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Transformation of Masked Benzyl Alcohols to *o*-Aminobenzaldehydes through C-H Activation: A Facile Approach to Quinazolines

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Supporting Information

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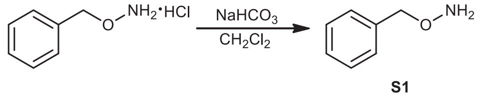
1. Reagents: Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Column chromatography purifications were performed using 300–400 mesh silica gel.

2. Instruments: NMR spectra were recorded on Varian Inova–400 MHz, Inova–300 MHz, Bruker DRX–400 or Bruker DRX–500 instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, br s = broad singlet, m = multiplet. HRMS analysis were carried out using a Bruker micrOTOF–Q instrument or a TOF–MS instrument.

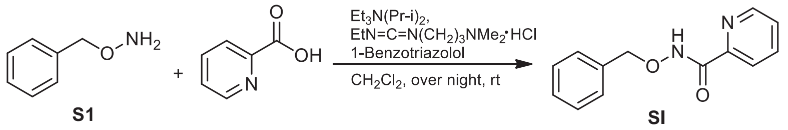
3. Preparation of masked benzyl alcohol substrates

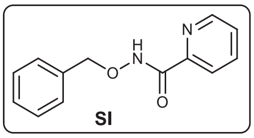
Preparation of Benzylhydroxylamine substrates S1



To a beaker of *o*-Benzoylhydroxylamine hydrochloride (4.79 g, 30 mmol, 1.0 eq) was added a solution of saturated sodium bicarbonate at room temperature until the effervescence ended. The organic material was extracted three times with CH_2Cl_2 (25 ml per extraction). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give *o*-Benzoylhydroxylamine (**S1**).

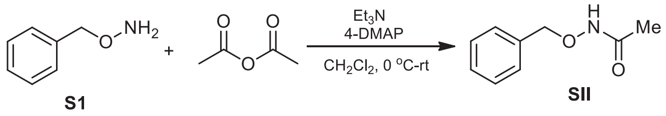
3.1 Preparation of SI[1]

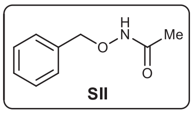




A mixture of **S1** (10 mmol, 1.0 eq), picolinic acid (1.1 eq), EDCI (1.1 eq), HOBt.H₂O (1.1 eq), and DIPEA (3.0 eq) in anhydrous DCM (40 mL) was stirred at room temperature over night. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give the desired product. Compound **SI** was prepared in 87% yield as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (br s, 1H), 8.43 (d, *J* = 4.1 Hz, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.83 (m, 1H), 7.45 – 7.42 (m, 2H), 7.41 – 7.31 (m, 4H), 5.04 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.04, 149.11, 148.28, 137.50, 135.33, 129.27, 128.80, 128.66, 126.75, 122.45, 78.63. HRMS Calcd for $C_{13}H_{12}N_2O_2$ $[M+H]^+$: 229.0977; Found: 229.0981.

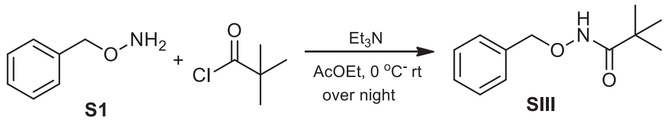
3.2 Preparation of SII[2]

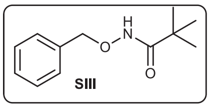




To a solution of **S1** (10 mmol, 1.0 eq) in DCM (40 mL) was added triethylamine (1.5 mL, 11 mmol) and 4-(dimethylamino)pyridine (1 mmol, 0.1 eq) at 0 °C. Acetic anhydride (1.0 mL, 11 mmol) was added dropwise, and the mixture was stirred for 10 min at 0 °C and 30 min at room temperature. The reaction was washed with saturated aqueous $NaHCO_3$, 1 M HCl, water, and brine. The organic layers was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*, purified by flash column chromatography on silica gel to give the product **SII**, yield 78% as colourless oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (br s, 1H), 7.36 – 7.29 (m, 5H), 4.83 (s, 2H), 1.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.25, 135.35, 128.94, 128.45, 128.35, 77.86, 19.58. HRMS Calcd for $C_9H_{11}NNaO_2$ $[M+Na]^+$: 188.0687; Found: 188.0693.

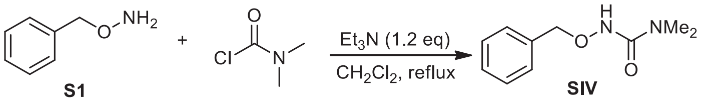
3.3 Preparation of SIII[3]

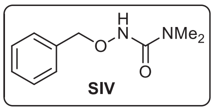




To a stirring solution of **S1** (10 mmol, 1.0 eq), Et$_3$N (1.5 mL, 11 mmol) in EtOAc (50 mL), was added trimethylacetyl chloride (1.5 mL, 41 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 10 minutes. Then, the reaction mixture was stirred at room temperature overnight. After that, the reaction mixture was extracted with EtOAc, washed with brine and dried over anhydrous Na$_2$SO$_4$. Then, the extract was concentrated *in vacuo* and purified by flash column chromatography on silica gel to give the product **SIII**, yield 76% as white solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.25 (br s, 1H), 7.41 – 7.34 (m, 5H), 4.90 (s, 2H), 1.15 (s, 9H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 176.19, 135.37, 129.54, 128.89, 128.70, 78.01, 38.16 , 27.30. HRMS Calcd for $C_{12}H_{17}NO_2$ $[M+H]^+$: 208.1338; Found: 208.1333.

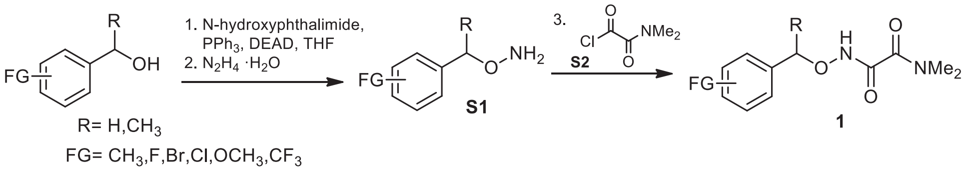
3.4 Preparation of SIV





A stirred mixture of **S1**(10.0 mmol), dimethylcarbamoyl chloride (1.62 g, 15 mmol) and Et$_3$N (2 mL) in CH$_2$Cl$_2$ (30 mL) was heated under reflux over night. The mixture was poured onto H$_2$O (25 mL) and the organic layer was separated, washed with H$_2$O (30 mL), brine (30 mL)and dried over anhydrous Na$_2$SO$_4$ and the solvent was removed *in vacuo*, purified by column chromatography on silica gel to give the product **SIV** ,Yield 70% as white solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (br s, 1H), 7.38 (dd, J = 7.8, 1.6 Hz, 2H), 7.34 – 7.29 (m, 3H), 4.82 (s, 2H), 2.79 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 159.64, 136.14, 128.77 , 128.14, 127.99, 77.76, 35.72. HRMS Calcd for $C_{10}H_{14}N_2O_2$ $[M+H]^+$: 195.1134; Found: 195.1139. HRMS Calcd for $C_{10}H_{14}N_2O_2$ $[M+H]^+$: 195.1134; Found: 195.1151.

4. General procedures for the preparation of (*N*,*N*-dimethyl)oxamoyl amide-protected benzyl alcohol substrates 1a–1r



4.1 Preparation of (*N*,*N*-dimethyl)oxamoyl chloride S2[4]

Step A: A solution of dimethylamine hydrochloride (4.89 g, 60 mmol, 1.0 eq) in CH$_2$Cl$_2$ (50 mL) with triethylamine(10 mL, 72 mmol, 1.2 eq), which need to add CH$_2$Cl$_2$ to make sure that dimethylamine hydrochloride was dissolved completely, was added dropwise to a solution of oxalyl chloride (7.5 ml, 90 mmol, 1.5 eq) in CH$_2$Cl$_2$ (100 mL) at 0 °C. The solution was warmed to room temperature and stirred over night. The excess of oxalylchloride and the solvent were removed *in vacuo*, CH$_2$Cl$_2$ (60 mL) was added and evaporated. This operation was performed twice to give **S2** as a pale yellow solid. The crude product was used in the next step without further operation.

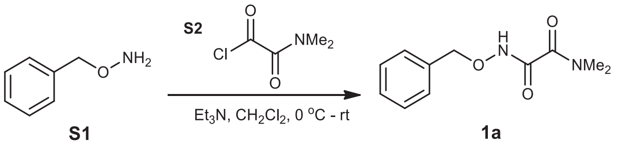
4.2 Preparation of Benzylhydroxylamine substrates S1[5]

Step B: To a solution of benzyl alcohol (20 mmol, 1.0 eq), N-hydroxyphthalimide (22 mmol, 1.1 eq) and PPh$_3$ (22 mmol, 1.1 eq) in 40 mL anhydrous THF was added diethyl azodicarboxylate (22 mmol, 1.1 eq) dropwise over 5 minutes at room temperature. The reaction was monitored by TLC (silica gel, eluent: EtOAc/ petroleum ether = 1:2) and usually completed in 3 hours. Then hydrazine monohydrate (24 mmol, 1.2 eq) wad added dropwise to the reaction mixture. The reaction was monitored by TLC (silica gel, eluent: EtOAc/petroleum ether=1:2) and usually completed in 30 minutes. On completion of the reaction, the mixture was filtered and silica gel (7.0 g) was added to the filtrate. After removal of the solvent *in vacuo*, the residue was purified by flash column chromatography on silica gel to give the product **S1**.

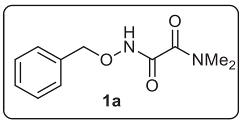
4. 3 preparation of marked benzyl alcohol substrates 1b–1r

Step C: A solution of (*N*,*N*-dimethyl)oxamoyl chloride **S2** (30 mmol, 1.5 eq) in CH_2Cl_2 (50 mL) was added dropwise to a solution of the title compound **S1** from **Step B** with triethylamine (3.0 ml, 21 mmol, 1.1 eq) in CH_2Cl_2 (40 mL) at 0 °C, and then the mixture was stirred at room temperature, over night before quenched by water (50 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL × 2). The combined organic layers were washed with brine (30 mL) and dried over anhydrous Na_2SO_4. After removal of the solvent *in vacuo*, purified by column chromatography on silica gel to give the product as white solid or colorless vitreous fluid.

4. 4 preparation of masked benzyl alcohol substrates 1a

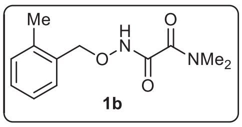


To a beaker of *o*-Benzoylhydroxylamine hydrochloride (4.79 g, 30 mmol, 1.0 eq) was added a solution of saturated sodium bicarbonate at room temperature until the effervescence ended. The organic material was extracted three times with CH_2Cl_2 (25 ml per extraction). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give *o*-Benzoylhydroxylamine (**S1**). Then according to the **step C** to get the compound **1a** as white solid, Yield 5.3 g, 80 %.



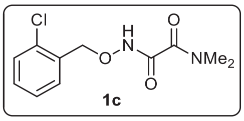
1a

Compound **1a** : white solid. Yield 80%. ^1H NMR (400 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 7.42 (dd, *J* = 7.2, 1.9 Hz, 2H), 7.35 – 7.32 (m, 3H), 4.93 (s, 2H), 3.18 (s, 3H), 2.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.26, 159.10, 134.86, 129.38, 128.98, 128.69, 78.50, 38.08, 36.46. HRMS Calcd for $C_{11}H_{14}N_2O_3$ $[M+H]^+$: 223.1083; Found: 223.1092.



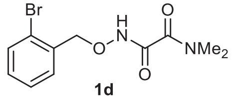
1b

Compound **1b**: white solid. Yield 50%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (br s, 1H), 7.38 – 7.30 (m, 2H), 6.97 – 6.88 (m, 2H), 5.02 (s, 2H), 3.85 (s, 3H), 3.31 (s, 3H), 2.96 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.19, 158.80, 158.22, 131.49, 130.61, 123.24, 120.62, 110.76, 73.78, 55.64, 38.13, 36.57. HRMS Calcd for $C_{12}H_{16}N_2O_3$ $[M+H]^+$: 237.1239, Found: 237.1249.



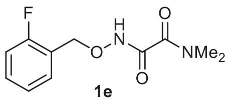
1c

Compound **1c** : white solid. Yield 63%. ^1H NMR (400 MHz, $CDCl_3$) δ 9.69 (br s, 1H), 7.54 – 7.49 (m, 1H), 7.42 – 7.38 (m, 1H), 7.32 – 7.28 (m, 2H), 5.11 (s, 2H), 3.34 (s, 3H), 2.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.88, 159.14, 134.59, 132.76, 131.30, 130.43, 129.81, 127.13, 75.46, 38.18, 36.73. HRMS Calcd for $C_{11}H_{13}ClN_2O_3$ $[M+H]^+$: 257.0693; Found: 257.0701.



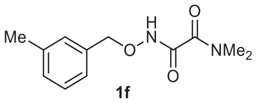
1d

Compound **1d** : white solid. Yield 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (br s, 1H), 7.46 (t, *J* = 6.9 Hz, 1H), 7.35 (dd, *J* = 13.1, 6.3 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.07 (t, *J* = 9.0 Hz, 1H), 5.03 (s, 2H), 3.32 (s, 3H), 2.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.02 , 159.15, 134.51 , 133.03, 131.23, 130.42, 127.73, 124.36, 77.54, 38.16, 36.64. HRMS Calcd for $C_{11}H_{13}BrN_2O_3$ $[M+H]^+$: 301.0188; Found: 301.0196.



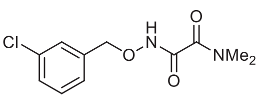
1e

Compound **1e** : white solid. Yield 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.21 (br s, 1H), 7.45 (t, *J* = 7.1 Hz, 1H), 7.35 – 7.28 (m, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 9.1 Hz, 1H), 5.00 (s, 2H), 3.24 (s, 3H), 2.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ161.47 (d, $J_{C\text{-}F}$ = 247.0 Hz), 161.35, 159.21, 131.83 (d, $J_{C\text{-}F}$ = 4.0 Hz), 130.90 (d, $J_{C\text{-}F}$ = 8.0 Hz), 124.26 (d, $J_{C\text{-}F}$ = 3.0 Hz), 122.17 (d, $J_{C\text{-}F}$ = 14.0 Hz), 115.51 (d, $J_{C\text{-}F}$ = 21.0 Hz), 71.61, 37.98, 36.27. ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.88; HRMS Calcd for $C_{11}H_{13}FN_2O_3$ $[M+H]^+$: 241.0988; Found: 241.0998.



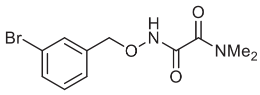
1f

Compound **1f**: colorless vitreous fluid. Yield 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02 (br s, 1H), 7.27 – 7.22 (m, 2H), 7.21 (d, *J* = 7.1 Hz, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 4.90 (s, 2H), 3.27 (s, 3H), 2.94 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.39, 159.10, 138.33, 134.73, 129.99, 129.65, 128.52, 126.35, 78.50, 38.01, 36.33 , 21.36. HRMS Calcd for $C_{12}H_{16}N_2O_3$ $[M+H]^+$: 237.1239; Found: 237.1244.



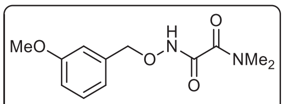
1g

Compound **1g** : white solid. Yield 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.12 (br s, 1H), 7.41 (s, 1H), 7.32 – 7.28 (m, 3H), 4.90 (s, 2H), 3.28 (s, 3H), 2.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.22, 159.19, 136.99, 134.50, 129.99, 129.19, 129.03, 127.28, 77.54, 38.09, 36.48. HRMS Calcd for $C_{11}H_{13}ClN_2O_3$ $[M+H]^+$: 257.0693; Found: 257.0701.



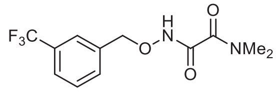
1h

Compound **1h** : white solid. Yield 47%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (br s, 1H), 7.62 (s, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.32 – 7.27 (m, 1H), 4.94 (s, 2H), 3.33 (s, 3H), 3.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.40, 159.18, 137.25, 131.99, 131.82, 130.17, 127.70, 122.50, 77.35, 38.00, 36.29 . HRMS Calcd for $C_{11}H_{13}BrN_2O_3$ $[M+H]^+$: 301.0188; Found: 301.0190.



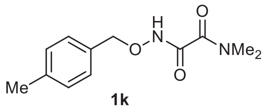
1i

Compound **1i** : colorless oily liquid. Yield 61%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.25 (br s, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 6.97 – 6.91 (m, 2H), 6.84 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.88 (s, 2H), 3.76 (s, 3H), 3.20 (s, 3H), 2.89 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.48, 159.71, 159.16, 136.38, 129.57, 121.35, 114.62, 114.23, 78.19, 55.25, 37.91, 36.13. HRMS Calcd for $C_{12}H_{16}N_2O_4$ [M+H]$^+$:253.1188; Found:253.1191.



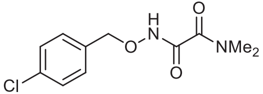
1j

Compound **1J** : white solid. Yield 45%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.21 (br s, 1H), 7.67 (s, 1H), 7.63 – 7.58 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 1H), 4.98 (s, 2H), 3.26 (s, 3H), 2.94 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.28, 159.34, 136.03, 132.51, 131.01 (q, $J_{C\text{-}F}$ = 33.0 Hz),129.22, 125.86 (d, $J_{C\text{-}F}$ = 3.0 Hz), 125.70 (d, $J_{C\text{-}F}$ = 3.0 Hz), 124.04 (q, $J_{C\text{-}F}$ = 270.0 Hz), 77.55, 38.05, 36.43. ^{19}F NMR (376 MHz, CDCl$_3$) δ -62.66. HRMS Calcd for $C_{12}H_{13}F_3N_2O_3$ [M+H]$^+$: 291.0957; Found: 291.0964.



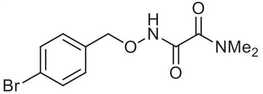
1k

Compound **1k** : white solid. Yield 43%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.55 (br s, 1H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 4.90 (s, 2H), 3.32 (s, 3H), 2.97 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.05 , 158.98, 139.00, 131.75, 129.51, 129.45, 78.44, 38.15, 36.64, 21.39. HRMS Calcd for $C_{12}H_{16}N_2O_3$ [M+H]$^+$: 237.1239; Found: 237.1246.



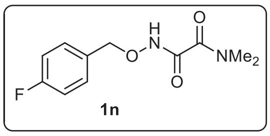
1l

Compound **1l** : white solid. Yield 66%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.86 (br s, 1H), 7.38 – 7.33 (m, 4H), 4.91 (s, 2H), 3.31 (s, 3H), 2.96 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.17, 159.15, 134.94, 133.41, 130.72, 128.89, 77.62, 38.11, 36.52. HRMS Calcd for $C_{11}H_{13}ClN_2O_3$ [M+H]$^+$: 257.0693; Found: 257.0700.

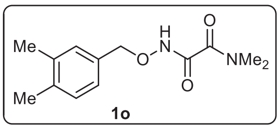


1m

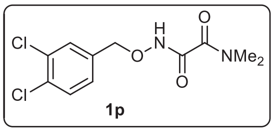
Compound **1m**: white solid. Yield 73%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.03 (br s, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 4.87 (s, 2H), 3.27 (s, 3H), 2.94 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.29, 159.17, 133.93, 131.79, 130.96, 123.07, 77.59, 38.07, 36.40. HRMS Calcd for $C_{11}H_{13}BrN_2O_3$ [M+H]$^+$: 301.0188; Found: 301.0196.


1n

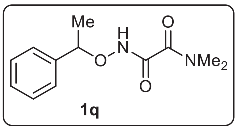
Compound **1n** : white solid. Yield 57%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.99 (br s, 1H), 7.40 (dd, *J* = 8.0, 5.7 Hz, 2H), 7.04 (dd, *J* = 12.0, 5.3 Hz, 2H), 4.89 (s, 2H), 3.27 (s, 3H), 2.94 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.94 (d, $J_{C\text{-}F}$ = 246.0 Hz), 161.61, 159.20, 131.24 (d, $J_{C\text{-}F}$ = 8.0 Hz), 130.79 (d, $J_{C\text{-}F}$ = 3.0 Hz), 115.37 (d, $J_{C\text{-}F}$ = 22.0 Hz), 77.43, 37.85, 36.01; ^{19}F NMR (376 MHz, CDCl$_3$) δ -112.85. HRMS Calcd for $C_{11}H_{13}FN_2O_3$ [M+H]$^+$: 241.0988; Found: 241.0996.


1o

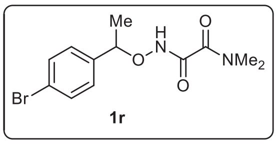
Compound **1o** : white solid. Yield 62%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.67 (br s, 1H), 7.18 (s, 1H), 7.12 (s, 2H), 4.87 (s, 2H), 3.31 (s, 3H), 2.96 (s, 3H), 2.25 (d, *J* = 1.2 Hz, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.18, 158.98, 137.57, 137.00, 132.15, 130.71, 129.94, 126.94, 78.48, 38.10, 36.53, 19.78, 19.67. HRMS Calcd for $C_{13}H_{18}N_2O_3$ [M+H]$^+$: 251.1396; Found: 251.1395.


1p

Compound **1p** : white solid. Yield 68%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.03 (br s, 1H), 7.46 (s, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.20 (d, *J* = 3.4 Hz, 1H), 4.82 (s, 2H), 3.24 (s, 3H), 2.90 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.15, 159.25, 135.23, 133.04, 132.75, 131.02, 130.69, 128.41, 38.11, 36.51. HRMS Calcd for $C_{11}H_{12}Cl_2N_2O_3$ [M+H]$^+$: 291.0303; Found: 291.0315.

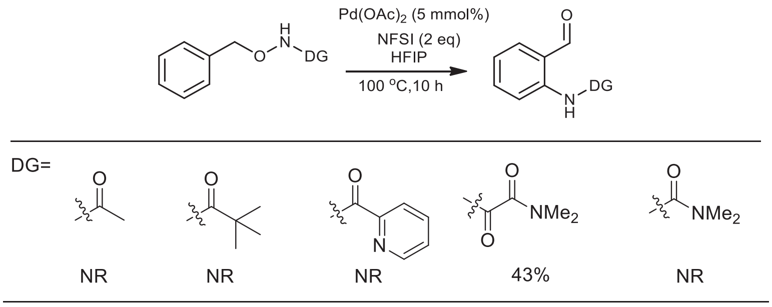

1q

Compound **1q** : white solid. Yield 70%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.54 (br s, 1H), 7.38-7.30 (m, 5H), 5.00 (q, *J* = 6.5 Hz, 1H), 3.20 (s, 3H), 2.89 (s, 3H), 1.58 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.32, 158.97, 140.41, 128.70, 128.64, 126.96, 83.95, 37.96, 36.30, 20.94. HRMS Calcd for $C_{12}H_{16}N_2O_3$ [M+H]$^+$: 237.1239; Found: 237.1248.


1r

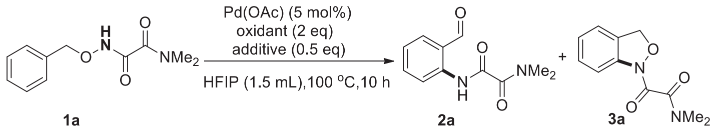
Compound **1r** : colorless vitreous fluid . Yield 73%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.11 (br s, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 4.98 (q, *J* = 6.5 Hz, 1H), 3.17 (s, 3H), 2.87 (s, 3H), 1.55 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.31, 159.03, 139.59, 131.78, 128.73, 122.53, 83.19, 37.99, 36.31, 20.87. HRMS Calcd for $C_{12}H_{15}BrN_2O_3$ [M+H]$^+$: 315.0344; Found: 315.0357.

5. Screening of directing groups.



[a] Reactions were carried out on a 0.2 mmol scale, using NFSI (2 eq) as an oxidant, using HFIP (1.5 mL) as the solvent. Yields were based on GC. NFSI = N-Fluorobenzenesulphonimide.

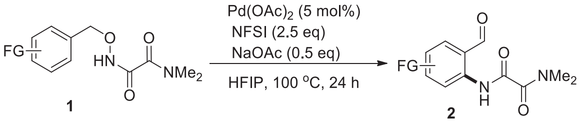
6. Screening of reaction conditions of intramolecular δ-C(sp^2)–H amination.[a]



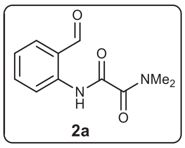
entry	oxidant	oxidant	additive	yield (%)[f,g]	
				2a :	**3a**
1	PhI(OAc)$_2$ (2 equiv)			0	12
2	$K_2S_2O_8$ (2 equiv)			16	30
3	NFSI (2 equiv)			43	56
4[b]	NFSI (2 equiv)			76	11
5[b]	NFSI (2.5 equiv)			80	10
6[b]	NFSI (2.5 equiv)		NaOAc	91(82)	3
7	H_2O_2 (4 equiv)			32	60
8	$K_2S_2O_8$ (2 equiv)	TBPB (4 equiv)		18	37
9	$K_2S_2O_8$ (2 equiv)	DTBP (4 equiv)		38	50
10	$K_2S_2O_8$ (2 equiv)	H_2O_2 (4 equiv)		25	68
11[c]	$K_2S_2O_8$ (2 equiv)	H_2O_2 (4 equiv)		0	0
12[d]	$K_2S_2O_8$ (2 equiv)	H_2O_2 (4 equiv)		22	32
13[e]	$K_2S_2O_8$ (2 equiv)	H_2O_2 (4 equiv)		10	17
14	$K_2S_2O_8$ (2 equiv)	H_2O_2 (4 equiv)	PivOH	14	80
15	$K_2S_2O_8$ (2 equiv)	H_2O_2 (4 equiv)	Ac-Val-OH	22	74
16	$K_2S_2O_8$ (2 equiv)	H_2O_2 (4 equiv)	PhCOOH	75	73
17	$K_2S_2O_8$ (2 equiv)	H_2O_2 (4 equiv)	DCB	7	89

Reaction conditions: [a] **1a** (0.1 mmol, 1.0 equiv), Pd(OAc)$_2$ (0.005 mmol), oxidant (0.2 mmol, 2.0 equiv), HFIP (1.5 mL), 100 °C, 10 h; [b] 24 h; [c] Without Pd(OAc)$_2$; [d] Using 1,4-dioxane as solvent; [e] Using DCE as solvent. [f] Yield was based on GC using tridecane as the internal standard. [g] Isolated yield. NFSI = N-Fluorobenzenesulphonimide. HFIP = hexafluoroisopropanol. TBPB = tert-butyl peroxybenzoate. DTBP = di-t-butylperoxide. H_2O_2 (35 wt.% solution in water). DCB= 3,5-dichlorobenzoic acid.

7. Palladium-Catalyzed Amination Using NFSI As An Oxidant.

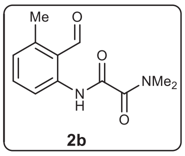


A mixture of **1** (0.2 mmol, 1.0 eq), Pd(OAc)$_2$ (2.2 mg, 0.05 eq), NFSI (157.6 mg, 0.5 mmol, 2.5 eq), NaOAc (8.2 mg, 0.1 mmol, 0.5 eq) and HFIP (3 mL) in a 25 mL glass vial sealed with PTFE cap was heated at 100 °C for 24 hours. The reaction mixture was cooled to room temperature, The crude reaction mixture was diluted with EtOAc (6 mL) and filtered on a pad of Celite. Then a spoon of silica gel (0.2 g) was added and the filtrate was concentrated *in vacuo*. The resulting residue was purified by column chromatography to give the product **2a-2p**.



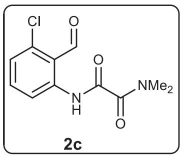
2a

Compound **2a:** white solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 12.32 (br s, 1H), 9.89 (s, 1H), 8.62 (d, *J* = 8.4 Hz, 1H), 7.66 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.21 (m, *J* = 7.5, 1.0 Hz, 1H), 3.36 (s, 3H), 3.02 (s, 3H);. ^{13}C NMR (101 MHz, CDCl$_3$) δ 194.64, 161.43, 160.13, 139.00, 136.03, 135.60, 123.85, 122.62, 119.62, 38.31, 37.21. HRMS Calcd for $C_{11}H_{12}N_2O_3$ $[M+H]^+$: 221.0926; Found: 221.0936.



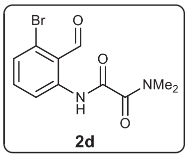
2b

Compound **2b:** white solid . ^{1}H NMR (400 MHz, CDCl$_3$) δ 12.77 (br s, 1H), 10.51 (s, 1H), 8.56 (d, *J* = 8.5 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 7.5 Hz, 1H), 3.41 (s, 3H), 3.10 (s, 3H), 2.68 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 193.81, 162.00, 160.52, 143.43, 140.04, 135.99, 127.02, 120.47, 118.53, 38.53, 37.41, 19.32. HRMS Calcd for $C_{12}H_{14}N_2O_3$ $[M+H]^+$: 235.1083; Found: 235.1084.



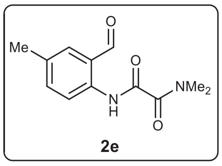
2c

Compound **2c:** white solid . ^{1}H NMR (400 MHz, CDCl$_3$) δ 12.81 (br s, 1H), 10.63 (s, 1H), 8.67 (d, *J* = 8.5 Hz, 1H), 7.53 (t, *J* = 8.3 Hz, 1H), 7.23 (dd, *J* = 8.0, 0.9 Hz, 1H), 3.43 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 193.57, 161.50, 160.44, 141.45, 140.42, 136.43, 125.81, 119.04, 118.80, 38.58, 37.62. HRMS Calcd for $C_{11}H_{11}ClN_2O_3$ $[M+H]^+$: 255.0536; Found: 255.0544.



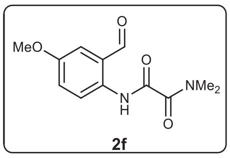
2d

Compound **2d:** white solid . ^{1}H NMR (400 MHz, CDCl$_3$) δ 12.81 (br s, 1H), 10.53 (s, 1H), 8.75 – 8.69 (m, 1H), 7.46 – 7.42 (m, 2H), 3.43 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 196.07, 161.48, 160.31, 141.50, 136.49, 130.03, 129.33, 119.79, 119.49, 38.58, 37.63. HRMS Calcd for $C_{11}H_{11}BrN_2O_3$ $[M+H]^+$: 299.0031; Found: 299.0045.



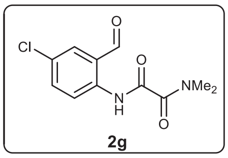
2e

Compound **2e:** white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.28 (br s, 1H), 9.91 (s, 1H), 8.57 (d, *J* = 8.5 Hz, 1H), 7.49 (d, *J* = 1.8 Hz, 1H), 7.41 (dd, *J* = 8.5, 2.0 Hz, 1H), 3.41 (s, 3H), 3.08 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.83, 161.79, 160.18, 136.86, 136.48, 136.41, 133.84, 122.84, 119.94, 38.51, 37.43, 20.65. HRMS Calcd for $C_{12}H_{14}N_2O_3$ $[M+H]^+$: 235.1083; Found: 235.1093.



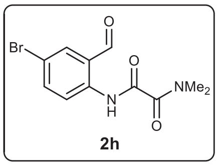
2f

Compound **2f:** white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.16 (br s, 1H), 9.94 (s, 1H), 8.66 (d, *J* = 9.0 Hz, 1H), 7.22 (d, *J* = 3.0 Hz, 1H), 7.18 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.88 (s, 3H), 3.44 (s, 3H), 3.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.35, 161.88, 159.93, 155.99, 132.78, 123.91, 121.73, 121.54, 120.02, 55.87, 38.58, 37.52. HRMS Calcd for $C_{12}H_{14}N_2O_4$ $[M+H]^+$: 251.1032; Found: 251.1039.



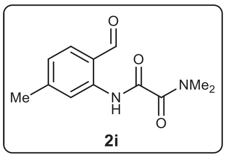
2g

Compound **2g:** white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.38 (br s, 1H), 9.93 (s, 1H), 8.71 (d, *J* = 9.0 Hz, 1H), 7.70 (d, *J* = 2.5 Hz, 1H), 7.59 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.45 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.46, 161.29, 160.20, 137.80, 135.67, 135.31, 129.25, 123.96, 121.54, 38.60, 37.70. HRMS Calcd for $C_{11}H_{11}ClN_2O_3$ $[M+H]^+$: 255.0536; Found: 255.0537.



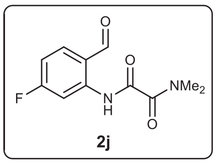
2h

Compound **2h:** white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.39 (br s, 1H), 9.92 (s, 1H), 8.65 (d, *J* = 8.9 Hz, 1H), 7.84 (d, *J* = 2.4 Hz, 1H), 7.73 (dd, *J* = 8.9, 2.3 Hz, 1H), 3.45 (s, 3H), 3.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.41, 161.28, 160.21, 138.57, 138.33, 138.25, 124.28, 121.76, 116.43, 38.61, 37.71. HRMS Calcd for $C_{11}H_{11}BrN_2O_3$ $[M+H]^+$: 299.0031; Found: 299.0034.



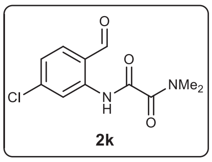
2i

Compound **2i:** white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.42 (br s, 1H), 9.92 (s, 1H), 8.56 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 7.1 Hz, 1H), 3.43 (s, 3H), 3.11 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.22, 161.81, 160.46, 147.62, 139.33, 136.29, 125.01, 120.93, 120.45, 38.57, 37.51, 22.55. HRMS Calcd for $C_{12}H_{14}N_2O_3$ $[M+H]^+$: 235.1083; Found: 2235.1093.



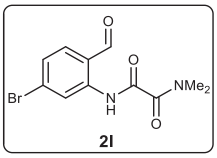
2j

Compound **2j:** white solid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.62 (br s, 1H), 9.93 (s, 1H), 8.51 (dd, J = 11.6, 2.1 Hz, 1H), 7.73 (dd, J = 8.5, 6.2 Hz, 1H), 6.98 (m, 1H), 3.45 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.27, 167.05 (d, J_{C-F} = 256.0 Hz), 161.20, 160.48, 141.65 (d, J_{C-F} = 14.0 Hz), 138.57 (d, J_{C-F} = 12.0 Hz), 119.75 (d, J_{C-F} = 2.0 Hz), 111.36 (d, J_{C-F} = 23.0 Hz), 107.63 (d, J_{C-F} = 29.0 Hz), 38.58, 37.66; ^{19}F NMR (376 MHz, $CDCl_3$) δ -98.05. HRMS Calcd for $C_{11}H_{11}FN_2O_3$ $[M+H]^+$: 239.0832; Found: 239.0840.



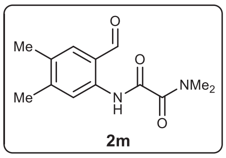
2k

Compound **2k:** white solid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.51 (br s, 1H), 9.93 (s, 1H), 8.98 (d, J = 1.4 Hz, 1H), 7.57 (d, J = 8.2 Hz, 1H), 7.45 (dd, J = 8.2, 1.8 Hz, 1H), 3.45 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.81, 161.17, 160.28, 140.03, 137.04, 131.43, 127.35, 123.07, 121.57, 38.63, 37.74. HRMS Calcd for $C_{11}H_{11}ClN_2O_3$ $[M+H]^+$: 255.0536; Found: 255.0550.



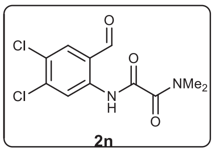
2l

Compound **2l:** white solid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.53 (br s, 1H), 9.94 (s, 1H), 8.81 (d, J = 1.8 Hz, 1H), 7.66 (d, J = 8.2 Hz, 1H), 7.28 (dd, J = 8.5, 1.4 Hz, 1H), 3.45 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.59, 161.18, 160.33, 142.59, 140.18, 137.05, 124.34, 121.25, 120.14, 38.62, 37.72. HRMS Calcd for $C_{11}H_{11}BrN_2O_3$ $[M+H]^+$: 299.0031; Found: 299.0042.



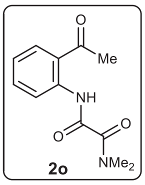
2m

Compound **2m:** white solid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.31 (br s, 1H), 9.89 (s, 1H), 8.52 (s, 1H), 7.43 (s, 1H), 3.43 (s, 3H), 3.10 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.33, 161.93, 160.24, 146.17, 137.19, 136.93, 132.73, 121.22, 121.10, 38.55, 37.47, 20.84, 19.18. HRMS Calcd for $C_{13}H_{16}N_2O_3$ $[M+H]^+$: 249.1239; Found: 249.1253.



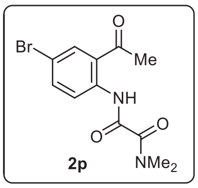
2n

Compound **2n:** white solid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.45 (br s, 1H), 9.90 (s, 1H), 8.95 (s, 1H), 7.78 (s, 1H), 3.46 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.56, 160.89, 160.12, 140.72, 138.10, 136.78, 127.73, 122.46, 121.96, 38.66, 37.86. HRMS Calcd for $C_{11}H_{10}Cl_2N_2O_3$ $[M+H]^+$: 289.0147; Found: 289.0151.



2o

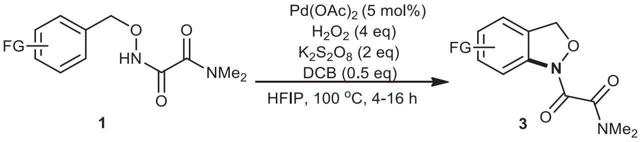
Compound **2o:** white solid . ^{1}H NMR (400 MHz, CDCl$_3$) δ 12.89 (br s, 1H), 8.76 (dd, *J* = 8.4, 0.6 Hz, 1H), 7.98 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.26 – 7.21 (m, 1H), 3.46 (s, 3H), 3.14 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.99, 162.21, 160.49, 139.44, 134.82, 131.75, 123.54, 123.28, 120.83, 38.48, 37.30, 28.60. HRMS Calcd for $C_{12}H_{14}N_2O_3$ [M+H]$^+$: 235.1083; Found: 235.1093.



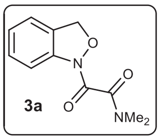
2p

Compound **2p:** white solid . ^{1}H NMR (400 MHz, CDCl$_3$) δ 12.94 (br s, 1H), 8.97 (d, *J* = 1.9 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.33 (dd, *J* = 8.5, 1.9 Hz, 1H), 3.43 (s, 3H), 3.10 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 201.21, 161.64, 160.35, 140.35, 132.76, 129.73, 126.66, 123.62, 121.73, 38.54, 37.52, 28.59. HRMS Calcd for $C_{12}H_{13}BrN_2O_3$ [M+H]$^+$: 313.0188; Found: 313.0200.

8. Palladium-catalyzed Intramolecular δ-C(sp^2)–H amination using two oxidants.

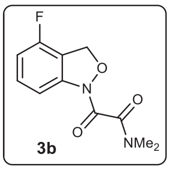


A mixture of **1** (0.2 mmol, 1.0 eq), Pd(OAc)$_2$ (2.2 mg, 0.05 eq), $K_2S_2O_8$ (241.6 mg, 2 eq), H_2O_2 (68.0 ul, 0.8 mmol, 4 eq) and HFIP (3 mL) in a 25 mL glass vial sealed with PTFE cap was heated at 100 °C or 110 °C for 4-16 hours. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica gel to give the product **3a-3l**.



3a

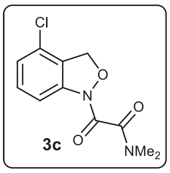
Compound **3a:** Pale yellow oily liquid . ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.85 (d, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.23 (dd, *J* = 12.1, 4.6 Hz, 2H), 5.47 (s, 2H), 3.08 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.94, 158.69, 134.99, 128.96, 127.88, 126.20, 121.65, 114.18, 73.51, 37.09, 33.80. HRMS Calcd for $C_{11}H_{12}N_2O_3$ [M+H]$^+$: 221.0926; Found: 221.0920.



3b

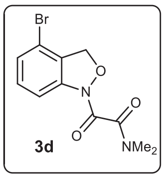
Compound **3b:** Yellow oily liquid .^{1}H NMR (400 MHz, CDCl$_3$) δ 7.62 (d, *J* = 7.5 Hz, 1H), 7.38–7.32 (m, 1H), 6.93 (t, *J* = 8.6 Hz, 1H), 5.51 (s, 2H), 3.08 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$)

δ 162.63, 159.03, 156.70 (d, $J_{C\text{-}F}$ = 247.0 Hz) ,137.45 (d, $J_{C\text{-}F}$ = 3.0 Hz), 131.42 (d, $J_{C\text{-}F}$ = 7.0 Hz), 114.60 (d, $J_{C\text{-}F}$ = 24.0 Hz), 113.22 (d, $J_{C\text{-}F}$ = 19.0 Hz), 110.08 (d, $J_{C\text{-}F}$ = 2.0 Hz), 71.33, 37.13, 33.90; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.90. HRMS Calcd for $C_{11}H_{11}FN_2O_3[M+H]^+$: 239.0832; Found: 239.0841.



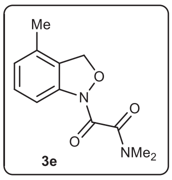
3c

Compound **3c:** Yellow oily liquid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 5.47 (s, 2H), 3.07 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.55, 159.10, 136.47, 130.72, 128.01, 126.50, 126.08, 112.32, 73.10, 37.11, 33.88. HRMS Calcd for $C_{11}H_{11}ClN_2O_3$ $[M+H]^+$: 255.0536; Found: 255.0539.



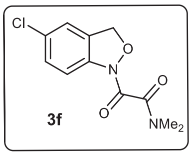
3d

Compound **3d:** Yellow oily liquid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.6 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.24 (t, J = 7.9 Hz, 1H), 5.42 (s, 2H), 3.07 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.46, 159.09, 136.19, 130.76, 128.78, 128.58, 115.48, 112.72, 74.37, 37.05, 33.82. HRMS Calcd for $C_{11}H_{11}BrN_2O_3$ $[M+H]^+$: 299.0031; Found: 299.0042.



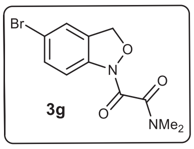
3e

Compound **3e:** Pale yellow oily liquid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.8 Hz, 1H), 7.27–7.23 (m, 1H), 7.00 (d, J = 7.6 Hz, 1H), 5.41 (s, 2H), 3.06 (s, 3H), 3.04 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.06, 158.66, 134.72, 132.20, 129.15, 127.25, 126.76, 111.57, 73.07, 37.13, 33.85, 18.68. HRMS Calcd for $C_{12}H_{14}N_2O_3[M+H]^+$: 235.1083; Found: 235.1089.

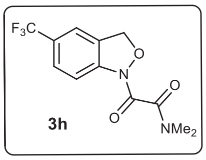


3f

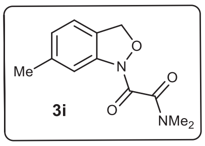
Compound **3f:** Yellow oily liquid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.3 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 7.23 (s, 1H), 5.44 (s, 2H), 3.07 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.65, 158.85, 133.94, 131.51, 129.77, 129.17, 122.12, 115.12, 73.12, 37.16, 33.93. HRMS Calcd for $C_{11}H_{11}ClN_2O_3$ $[M+H]^+$: 255.0536; Found: 255.0537.



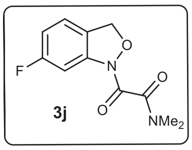
Compound **3g:** Yellow oily liquid . ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, *J* = 8.3 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.39 (s, 1H), 5.44 (s, 2H), 3.07 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.63, 158.89, 134.42, 132.07, 130.07, 124.99, 118.87, 115.48, 72.99, 37.16, 33.92. HRMS Calcd for $C_{11}H_{11}BrN_2O_3$ [M+H]$^+$: 299.0031; Found: 299.0040.



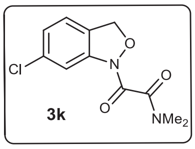
Compound **3h:** Yellow oily liquid .^{1}H NMR (400 MHz, CDCl$_3$) δ 7.92 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.52 (s, 1H), 5.52 (s, 2H), 3.08 (s, 3H), 3.06 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.36, 159.26, 137.81, 128.61 (q, $J_{C\text{-}F}$ = 32.0 Hz), 127.86 (d, $J_{C\text{-}F}$ = 6.0 Hz), 126.87 (q, $J_{C\text{-}F}$ = 3.0 Hz), 123.77(d, $J_{C\text{-}F}$ = 270.0 Hz), 119.21, 114.04, 73.20, 37.09, 33.88; ^{19}F NMR (376 MHz, CDCl$_3$) δ -61.97. HRMS Calcd for $C_{12}H_{11}F_3N_2O_3$ [M+H]$^+$: 289.0800; Found: 289.0813.



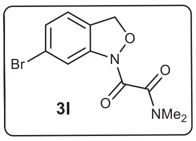
Compound **3i:** Pale yellow oily liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.68 (s, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 7.02 (d, *J* = 7.7 Hz, 1H), 5.41 (s, 2H), 3.06 (s, 3H), 3.04 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 163.04, 158.60, 139.42, 135.23, 126.97, 125.13, 121.28, 114.75, 73.52, 37.12, 33.85, 21.57. HRMS Calcd for $C_{12}H_{14}N_2O_3$ [M+H]$^+$: 235.1083; Found: 235.1088.



Compound **3j:** Brown oily liquid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.59 (d, *J* = 8.2 Hz, 1H), 7.18 (dd, *J* = 8.2, 4.9 Hz, 1H), 6.92 (m, 1H), 5.43 (s, 2H), 3.07 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ162.98 (d, $J_{C\text{-}F}$ = 245.0 Hz), 162.56, 158.91, 136.39 (d, $J_{C\text{-}F}$ = 12.0Hz), 123.19 (d, $J_{C\text{-}F}$ = 3.0 Hz), 122.59 (d, $J_{C\text{-}F}$ = 10.0 Hz), 113.01 (d, $J_{C\text{-}F}$ = 24.0 Hz), 102.68 (d, $J_{C\text{-}F}$ = 29.0 Hz), 73.37, 37.12, 33.88. ^{19}F NMR (376 MHz, CDCl$_3$) δ -111.63. HRMS Calcd for $C_{11}H_{11}FN_2O_3$ [M+H]$^+$: 239.0832; Found: 239.0838.



Compound **3k:** Brown oily liquid . ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.87 (s, 1H), 7.20 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 5.43 (s, 2H), 3.07 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.53, 158.97, 136.27, 134.95, 126.36, 126.27, 122.50, 114.58, 73.36, 37.14, 33.91. HRMS Calcd for $C_{11}H_{11}ClN_2O_3$ [M+H]$^+$: 255.0536; Found: 255.0548.

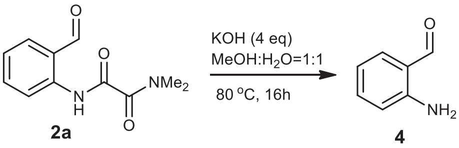


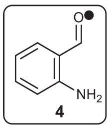
3l

Compound **3l:** Brown oily liquid .^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.35 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 5.41 (s, 2H), 3.07 (s, 3H), 3.05 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.47, 158.90, 136.33, 129.14, 126.95, 122.90), 122.47, 117.18, 73.37, 37.08, 33.85. HRMS Calcd for $C_{11}H_{11}BrN_2O_3$ $[M+H]^+$: 299.0031; Found: 299.0041.

9. The removal and transformation of directing group.

9.1 The removal of directing group [6]

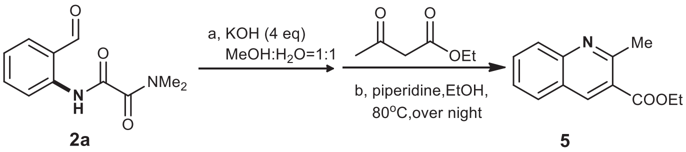


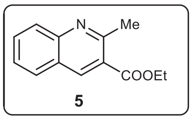


4

Compound **4: 2a** (66.0 mg, 0.3 mmol, 1.0 eq) was dissolved in a mixture of MeOH/H_2O (1:1) 2 mL, KOH (67.3 mg, 1.2 mmol, 4.0 eq) was then added. The mixture was heated to 80 °C and stirred for 16 hours. Water was added and the mixture was extracted with DCM. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to give the product **4** (30.9 mg, yield 88%), Pale yellow solid ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.29 (dd, *J* = 15.3, 7.8 Hz, 1H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.64 (d, *J* = 8.3 Hz, 1H), 6.14 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.16, 150.00, 135.79, 135.27, 118.86, 116.40, 116.09. C_7H_7NO CAS: 529-23-7.

9.2 Synthesis of quinoline or quinazoline derivatives 5, 6, 7, 8 through transformation of directing group.

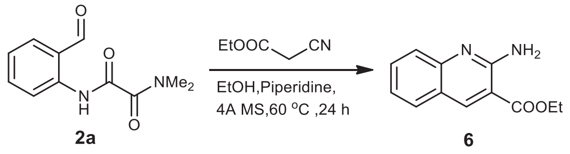


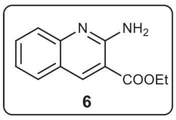


5

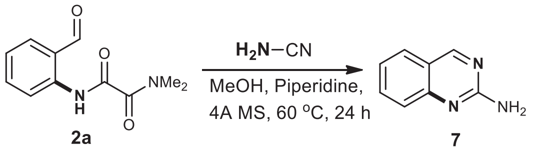
Compound **5**[7] **: Step A: 2a** (66.0 mg, 0.3 mmol, 1.0 eq) was dissolved in a mixture of MeOH/H_2O=1:1 (2 mL), KOH (67.3 mg, 1.2 mmol, 4.0 eq) was added. The mixture was heated to 80 °C and stirred for 16 hours. Water(1ml) was added and the mixture was extracted with DCM. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to give *o*-Aminobenzaldehyde**. Step B:** The title compound (30.9 mg, 0.26 mmol)from **step A** and molecular sieves 4 Å (0.1 g), absolute ethanol (1 mL), ethyl acetoacetate (40.0 uL, 0.31 mmol, 1.2 equiv) and piperidine in catalytic amount was stirred at 60 °C for 24 hours. The solution was diluted with CH_2Cl_2 and molecular sieves were filtered on a pad of Celite. The mixture was concentrated *in vacuo* and the resulting residue was purified by flash column chromatography to give the product **5** as a yellow solid (48.4 mg, yield 75 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.74 (m, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 2.97 (s, 3H), 1.43 (t, *J* =

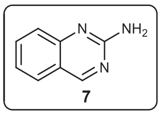
7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.50, 158.45, 148.61, 139.86, 131.63, 128.53, 128.46, 126.50, 125.75, 123.91, 61.38, 25.71, 14.35. HRMS Calcd for $C_{13}H_{13}NO_2$ $[M+H]^+$: 216.1025; Found: 216.1037. $C_{13}H_{13}NO_2$ CAS: 15785-08-7.



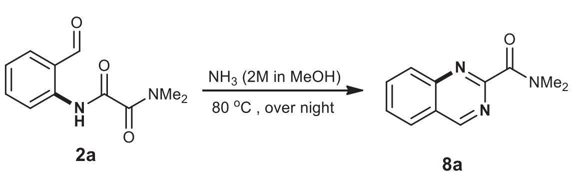


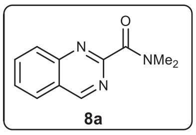
Compound **6**[8]: A mixture of **2a** (66.0 mg, 0.3 mmol, 1.0 equiv), molecular sieves 4 Å (0.1 g), absolute methanol (2 mL), ethyl cyanoacetate (38 uL, 0.36 mmol, 1.2 equiv) and piperidine in catalytic amount was stirred at 60 °C for 24 hours. The solution was diluted with CH_2Cl_2 and molecular sieves were filtered on a pad of Celite. The mixture was concentrated under vacuum and the resulting residue was purified by flash column chromatography to give the product **6** as a yellow solid (56.4 mg, yield 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.22 (m,1H), 6.67 (br s, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.65, 156.72, 150.23, 142.66, 132.62, 129.11, 125.63, 122.76, 122.47, 110.34, 61.42, 14.38. $C_{12}H_{12}N_2O_2$ CAS: 36926-83-7.





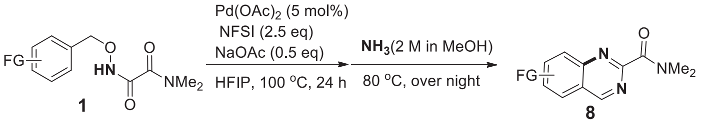
Compound **7**[8]**:** A mixture of **2a** (66.0 mg, 0.3 mmol, 1.0 equiv), molecular sieves 4 Å (0.1 g), absolute methanol (2 mL), cyanamide (24 uL, 0.36 mmol, 1.2 equiv) and piperidine in catalytic amount was stirred at 60 °C for 24 hours. The solution was diluted with CH_2Cl_2 and molecular sieves were filtered on a pad of Celite. The mixture was concentrated under vacuum and the resulting residue was purified by flash column chromatography to give the product **7** as a yellow solid (31.4 mg, yield 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 7.75 – 7.69 (m, 2H), 7.58 (d, *J* = 8.9 Hz, 1H), 7.32 – 7.27 (m, 1H), 5.29 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.69, 160.25, 152.06, 134.63, 127.70, 125.53, 123.44, 120.52. $C_8H_7N_3$ CAS :1687-51-0



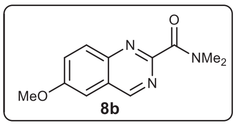


Compound **8a**[9]**:** A solution of Ammonia (2 M in methanol)(0.5 ml, 1.0 mmol) was dropwise with reusable syringe in a 25 ml glass vial with **2a** (66.0 mg, 0.3 mmol, 1.0 eq) at 0 °C in 5 mins. Then the tube was sealed and heated at 80 °C, over night. The mixture was cooled to room temperature and filtered on a pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography to give the product **8**, yield 92 % . Colorless oily liquid . ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.95 (t, *J* = 7.7 Hz, 2H), 7.70 (t, *J* = 7.5 Hz, 1H), 3.17 (s, 3H), 2.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.18, 161.00, 158.62, 149.78, 134.95, 128.80, 128.69, 127.32, 124.27, 38.46, 35.13. HRMS Calcd for $C_{11}H_{11}N_3O$ [M+H]$^+$: 202.0980; Found: 202.0989. $C_{11}H_{11}N_3O$ CAS:1373887-71-8.

10. Synthesis of quinazolines from benzyl alcohols in one pot.

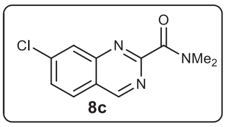


A mixture of (*N*,*N*-dimethyl)oxamoyl amide-protected benzyl alcohol substrate (0.3 mmol, 1.0 eq), $Pd(OAc)_2$ (2.2 mg, 0.05 eq), NFSI (156.7 mg, 0.75 mmol, 2.5 eq), NaOAc (12.3 mg, 0.15 mmol, 0.5 eq) and HFIP (4.5 mL) in a 25 mL glass vial sealed and heated at 100 °C for 24 hours. Then the reaction mixture was cooled to room temperature, a solution of 0.5 ml ammonia (2 M in methanol) was dropwised with reusable syringe at 0 °C in 5 mins, After stiring anther 5 mins, the glass vial was heated at 80 °C, over night. The mixture was cooled and filtered on a pad of Celite. The filtrate was concentrated *in vacuo*, and the resulting residue was purified by flash column chromatography to give the product **8a-8f** .



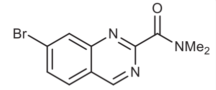
8b

Compound **8b:** Pale yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (s, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 7.61 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.18 (d, *J* = 2.7 Hz, 1H), 3.98 (s, 3H), 3.20 (s, 3H), 3.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.44, 159.39, 159.13, 156.80, 146.08, 130.29, 128.21, 125.53, 103.93, 55.99, 38.64, 35.33. HRMS Calcd for $C_{12}H_{13}N_3O_2$ [M+H]$^+$: 232.1086; Found: 232.1094.



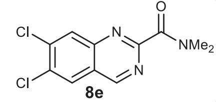
8c

Compound **8c:** White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 8.09 (d, *J* = 1.8 Hz, 1H), 7.94 (d, *J* = 8.7 Hz, 1H), 7.69 (dd, *J* = 8.7, 1.9 Hz, 1H), 3.21 (s, 3H), 3.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.84, 160.80, 159.50, 150.33, 141.43, 130.14, 128.64, 127.88, 122.65, 38.47, 35.21. HRMS Calcd for $C_{11}H_{10}ClN_3O$ [M+H]$^+$: 236.0591; Found: 236.0602.



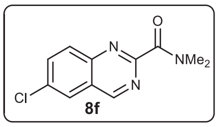
8d

Compound **8d:** White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 8.28 (d, *J* = 0.7 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.82 (dd, *J* = 8.7, 1.7 Hz, 1H), 3.20 (s, 3H), 2.99 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.84, 160.98, 159.47, 150.42, 132.69, 131.31, 130.04, 128.51, 122.90, 38.49, 35.23. HRMS Calcd for $C_{11}H_{10}BrN_3O$ [M+H]$^+$: 280.0085; Found: 280.0084.



8e

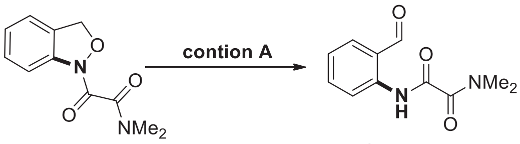
Compound **8e:** White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.22 (s, 1H), 8.10 (s, 1H), 3.20 (s, 3H), 2.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.60, 159.97, 159.51, 148.44, 140.40, 133.86, 130.08, 127.90, 123.18, 38.48, 35.26. HRMS Calcd for $C_{11}H_9Cl_2N_3O$ $[M+H]^+$: 270.0201; Found: 270.0214.



8f

Compound **8f:** White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.96 (d, *J* = 2.1 Hz, 1H), 7.88 (dd, *J* = 9.0, 2.3 Hz, 1H), 3.18 (s, 3H), 2.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.85, 160.09, 158.80, 148.30, 136.02, 134.64, 130.49, 126.01, 124.73, 38.48, 35.22. HRMS Calcd for $C_{11}H_{10}ClN_3O$ $[M+H]^+$: 236.0591; Found: 236.0600.

11. Preliminary mechanism study: role of NFSI

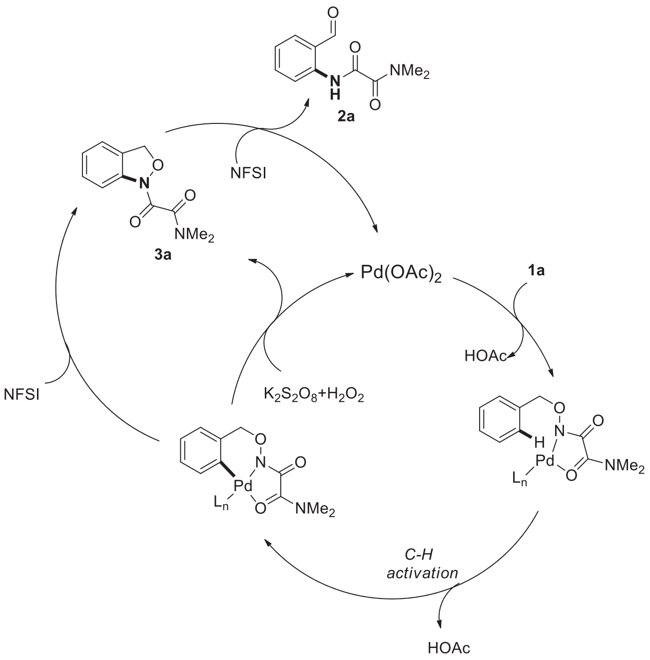


3a **2a**

Entry	Pd(OAc)$_2$	NFSI	NaOAc	GC Yield (%)
1	5 mol %	—	—	
2	—	2.5 eq	—	53
3	—	—	0.5 eq	0
4	5 mol %	2.5 eq	—	64
5	5 mol %	2.5 eq	0.5 eq	83
6[a]	—	2.5 eq	—	67
7[a]	—	2.5 eq	0.5 eq	80

Condition A: **3a** (0.1 mmol, 1eq), Pd(OAc) (0.005 mmol), NFSI (0.25 mmol, 2.5 eq), NaOAc (0.05 mmol, 0.5 eq), 12 h. [a] 24 h. Yield was base on GC using tridecane as the internal standard.

12. Proposed catalytic cycle for Palladium-catalyzed



13. References

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[5] K Guo, X. L. Chen, M. Y. Guan and Y. S. Zhao, *Org. Lett.* 2015, **17**, 1802−1805.

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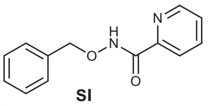
14. NMR spectra



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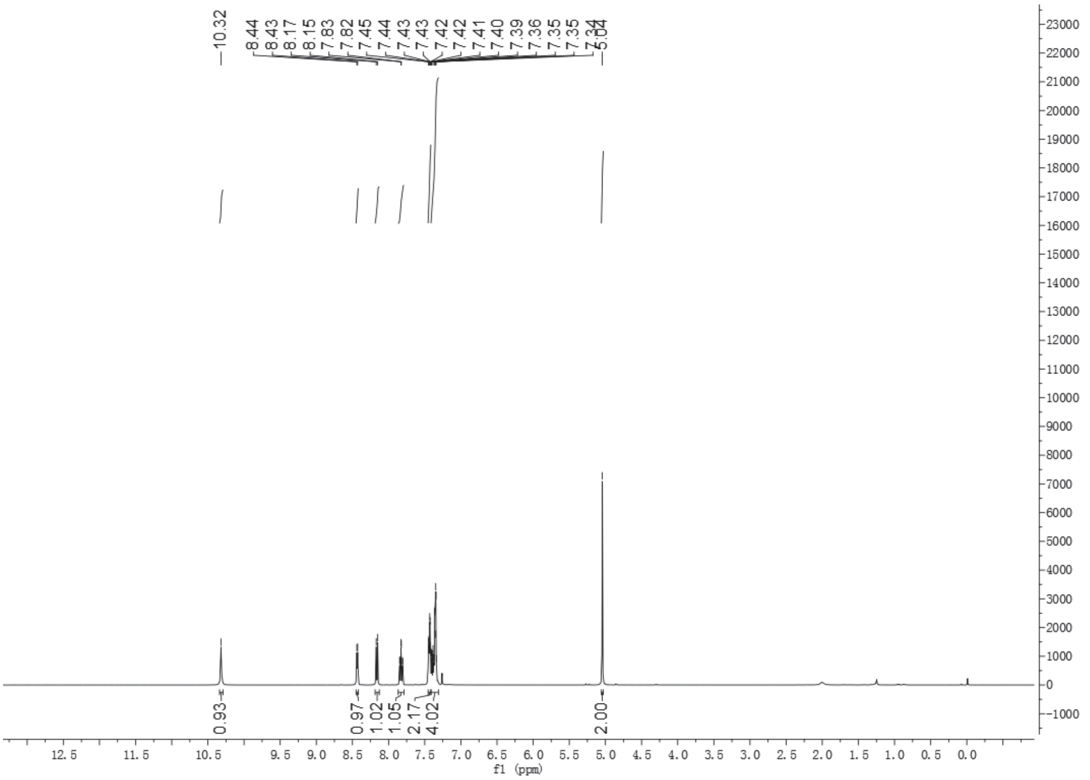

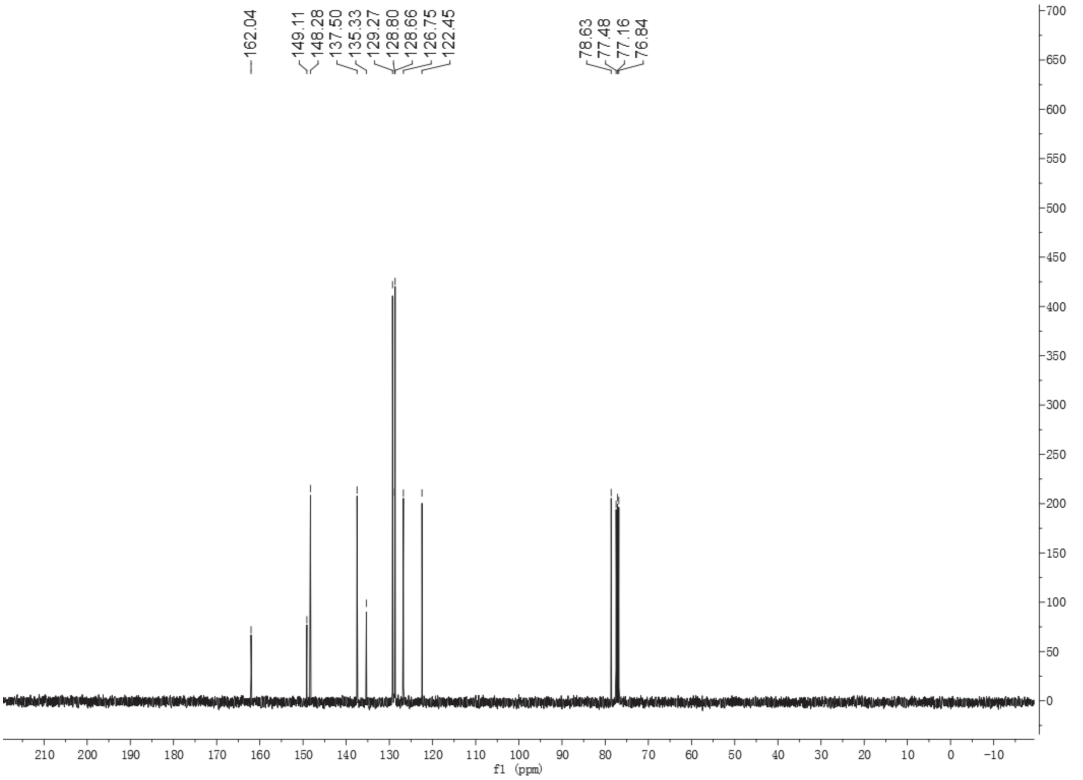

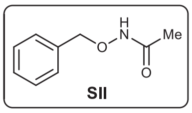
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O

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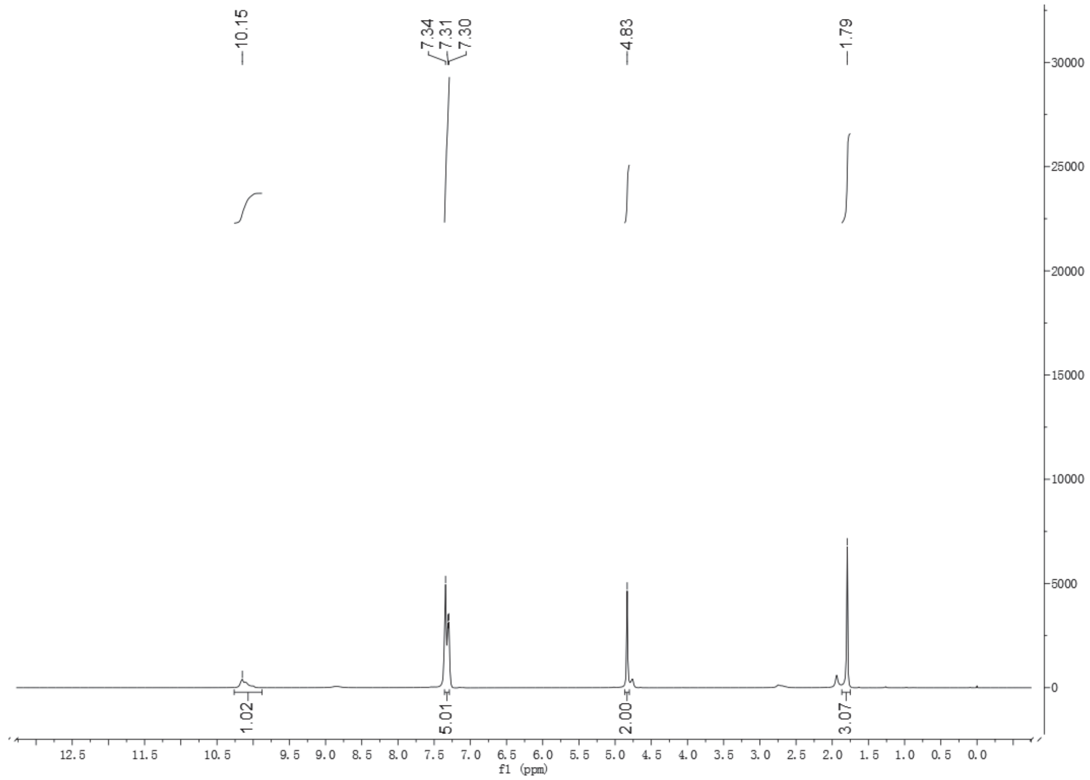
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10.5
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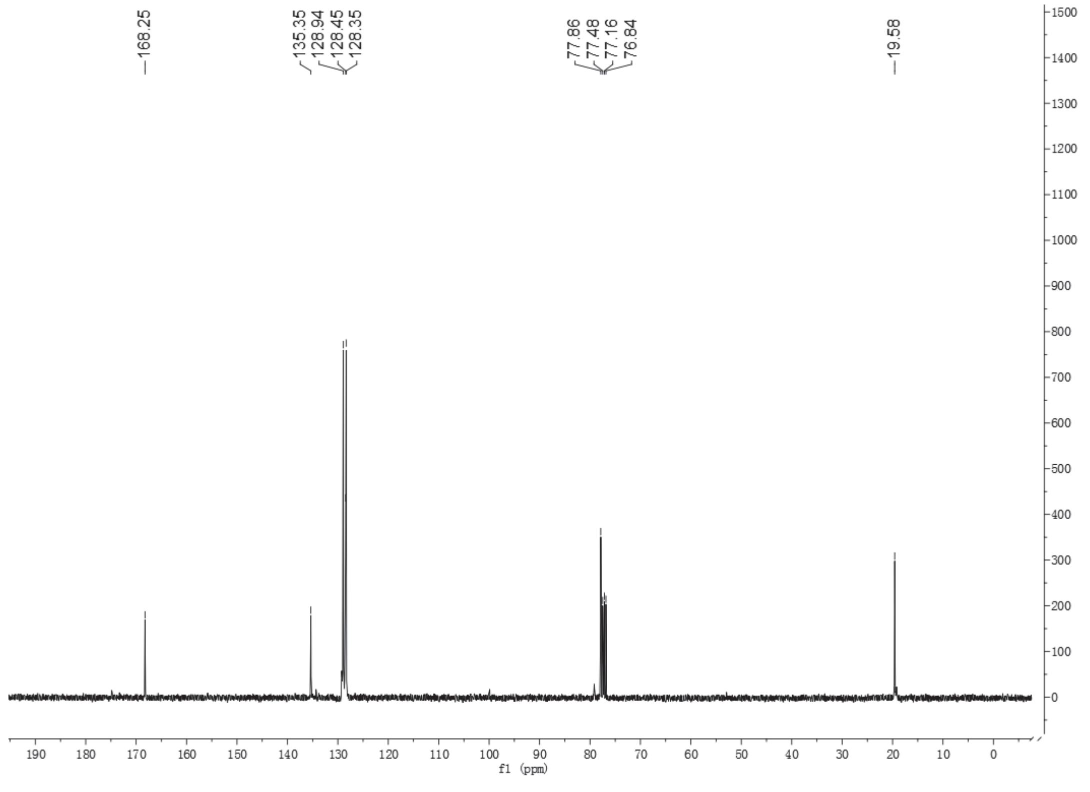
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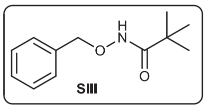

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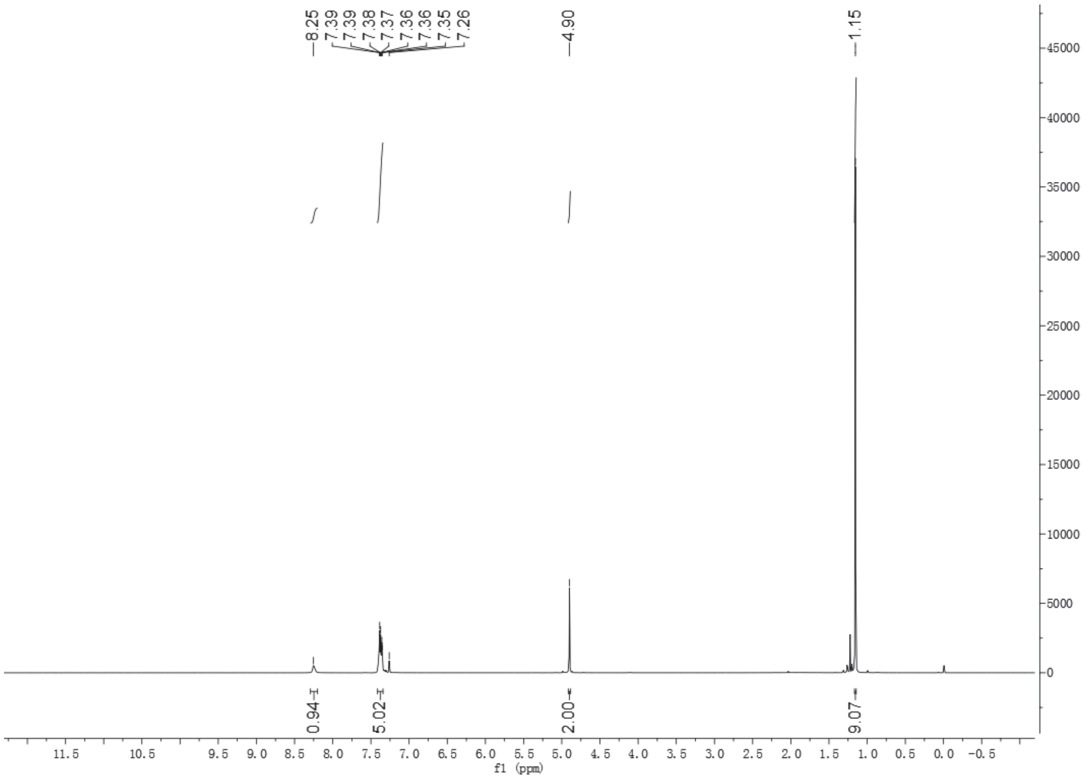
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30000
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20000
15000
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5000
0
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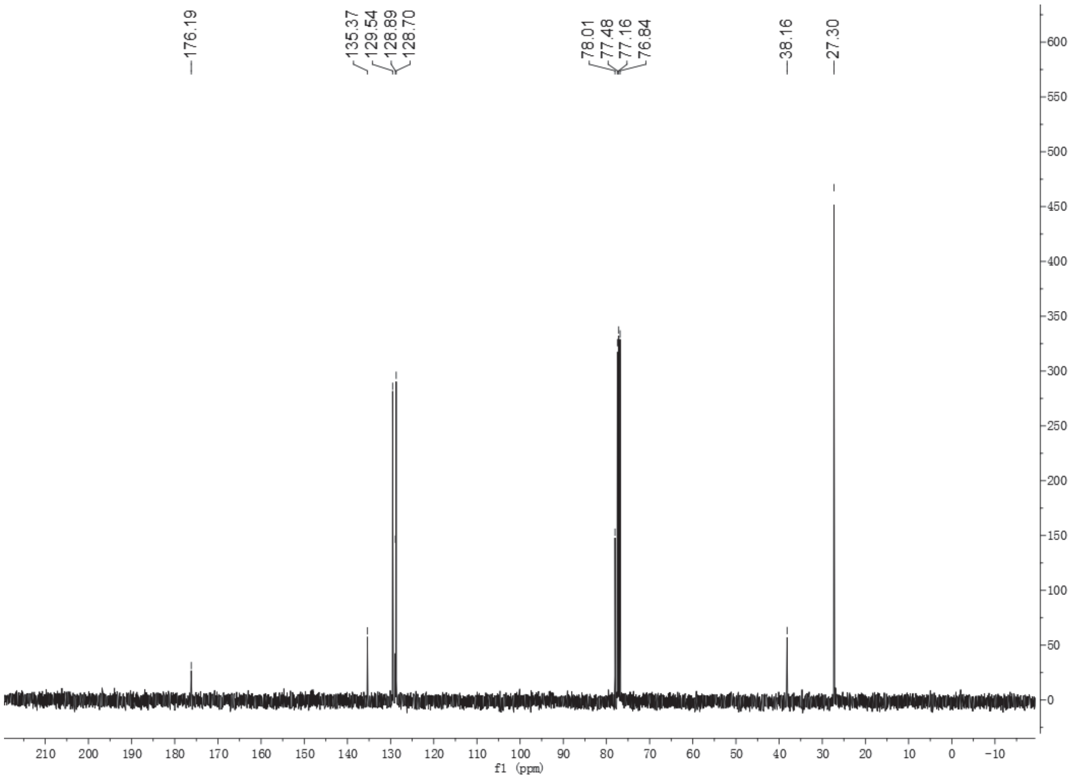
f1 (ppm)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38.16
27.30
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500
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200
150
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50
0
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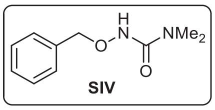
f1 (ppm)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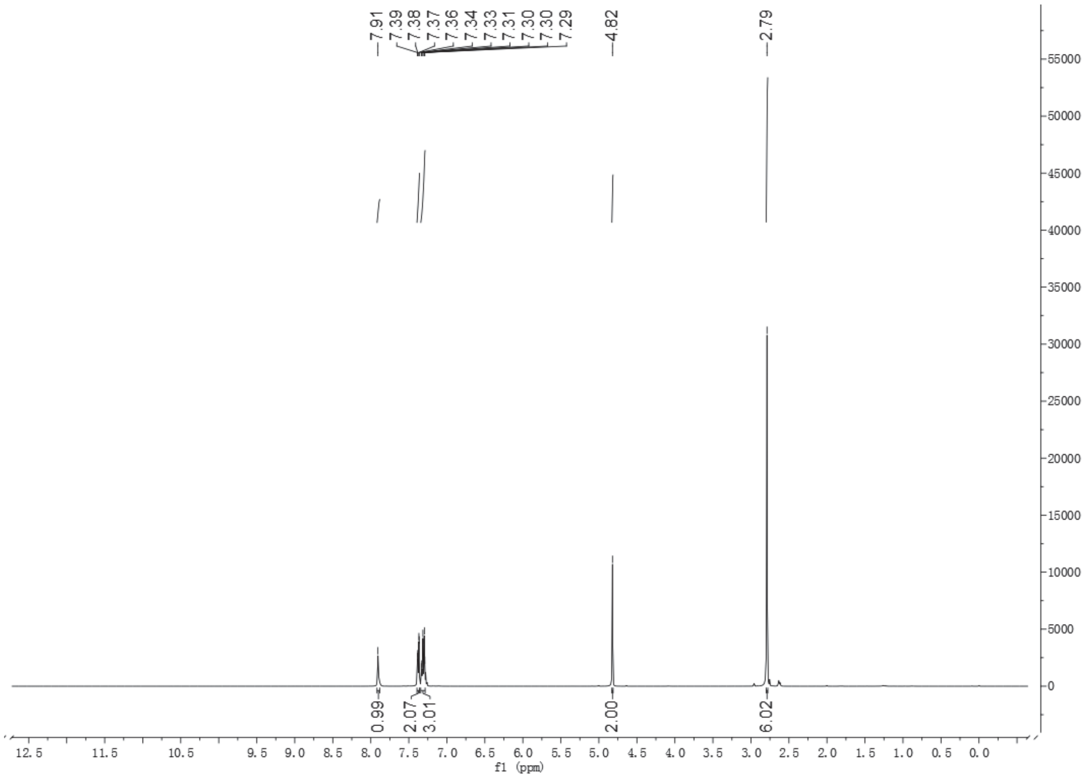
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40000
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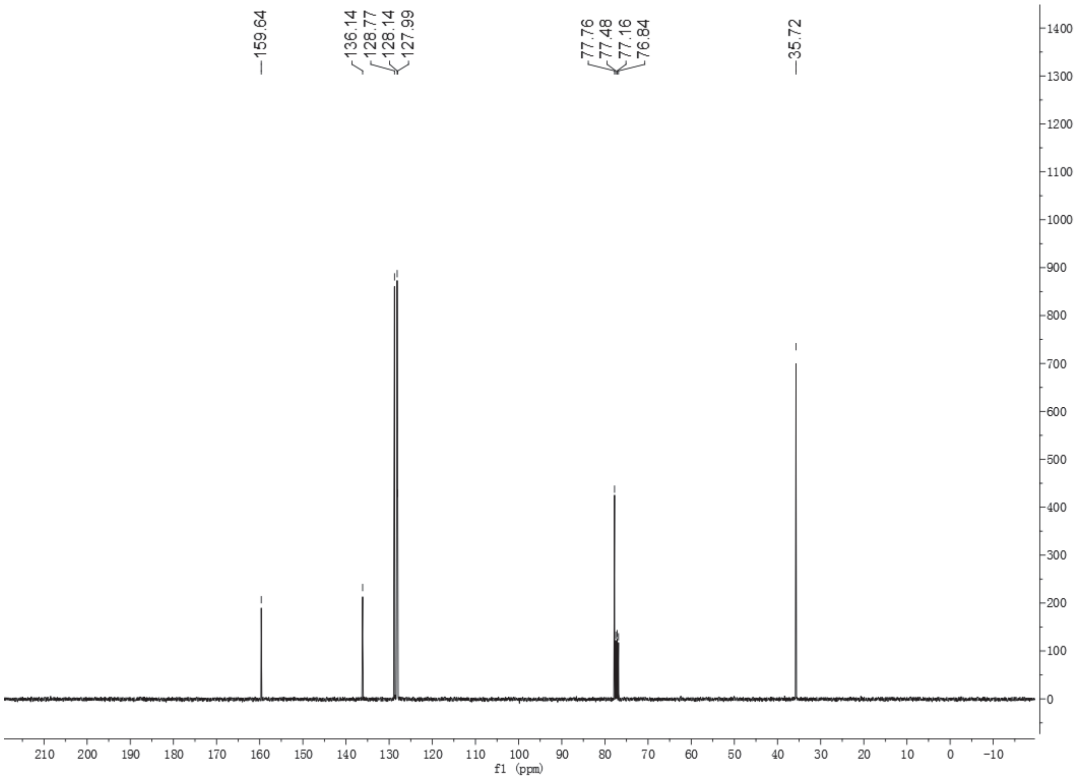
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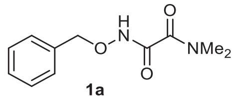
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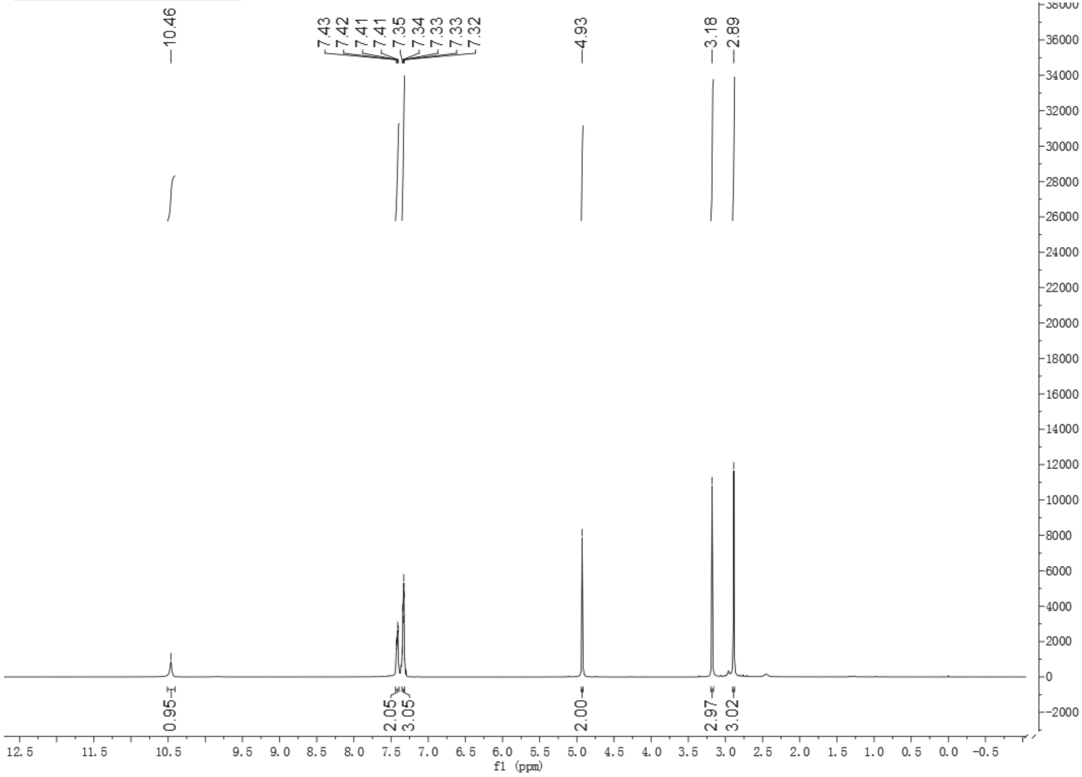
1a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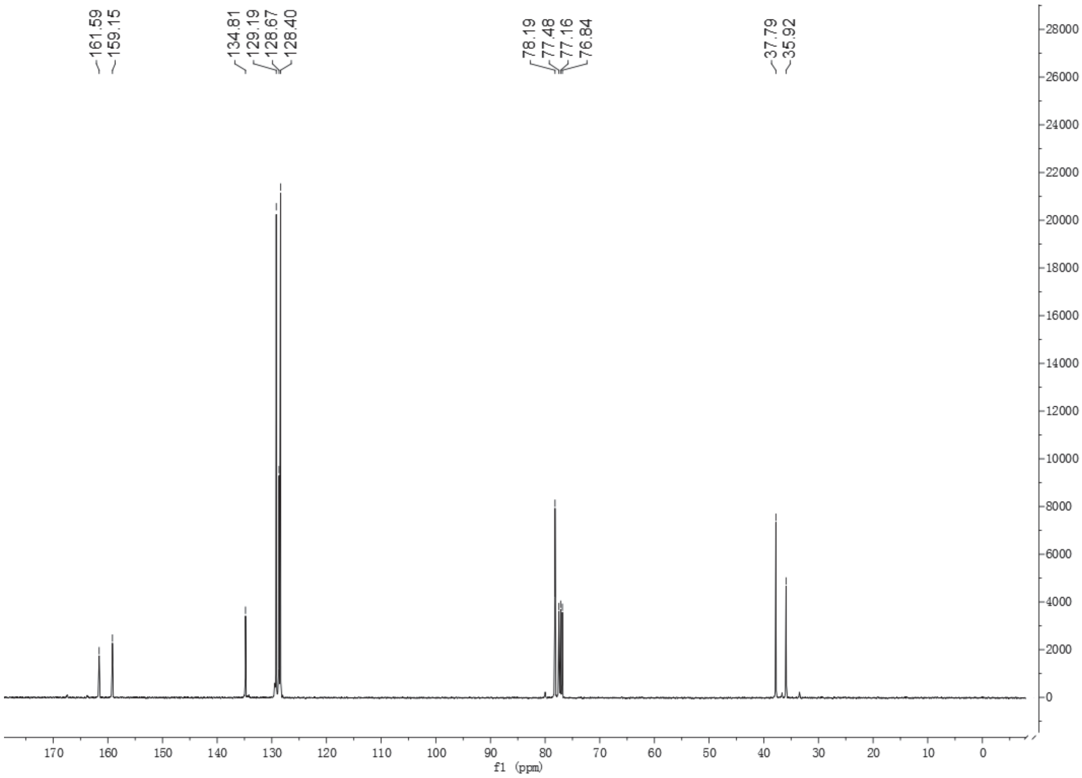
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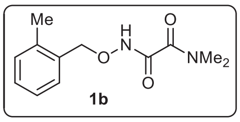
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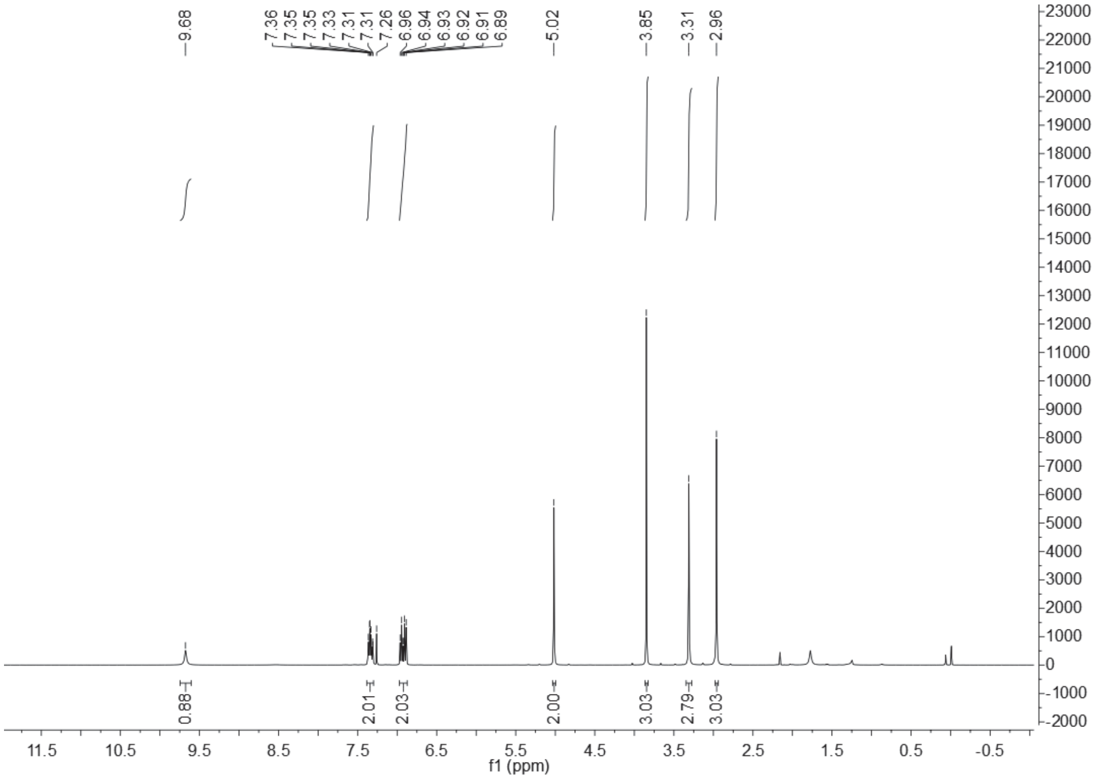
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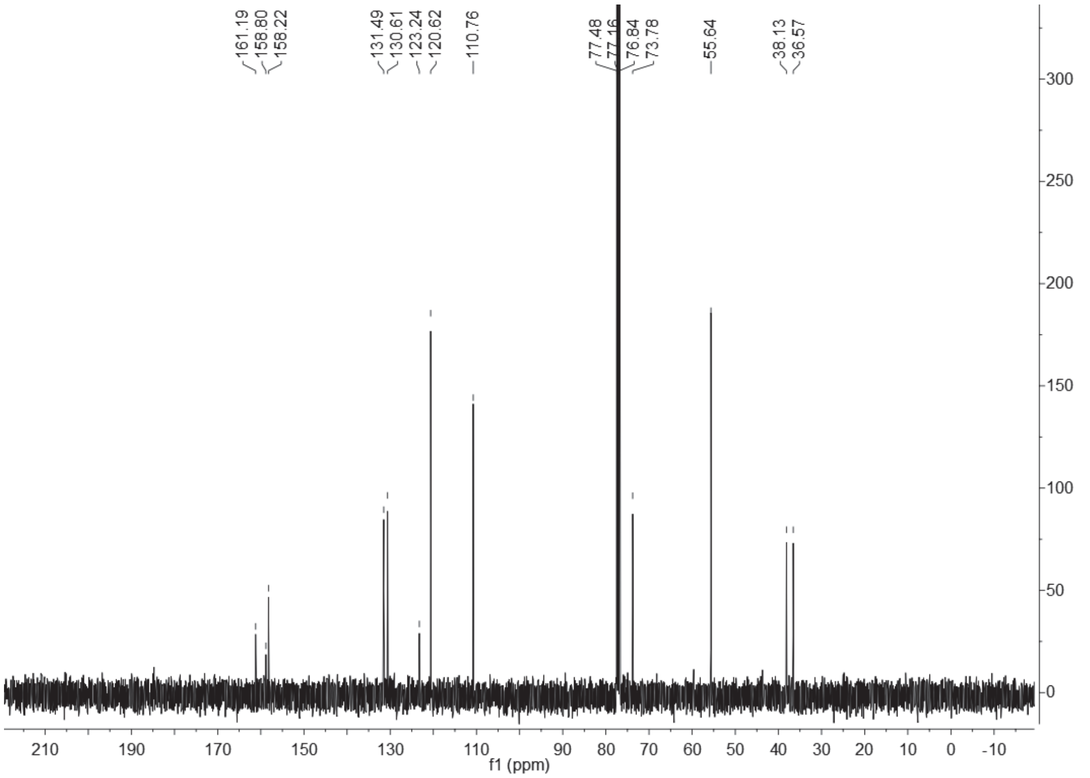
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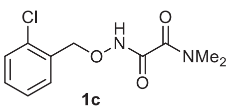
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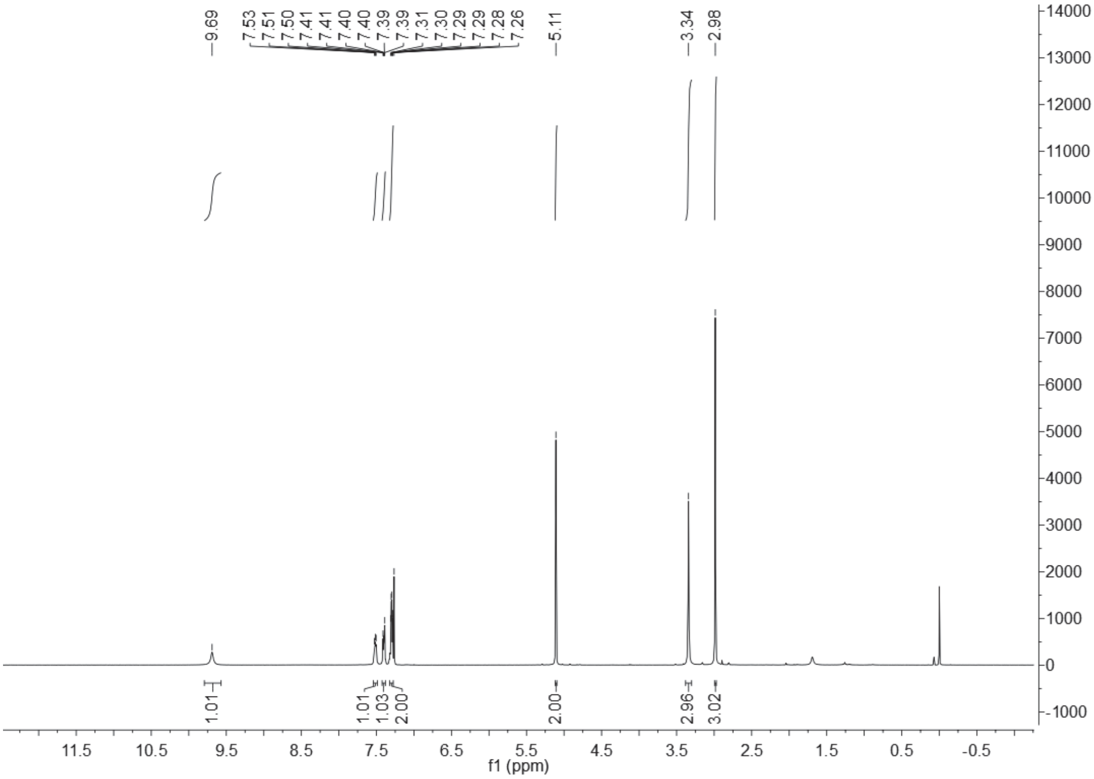
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2.96
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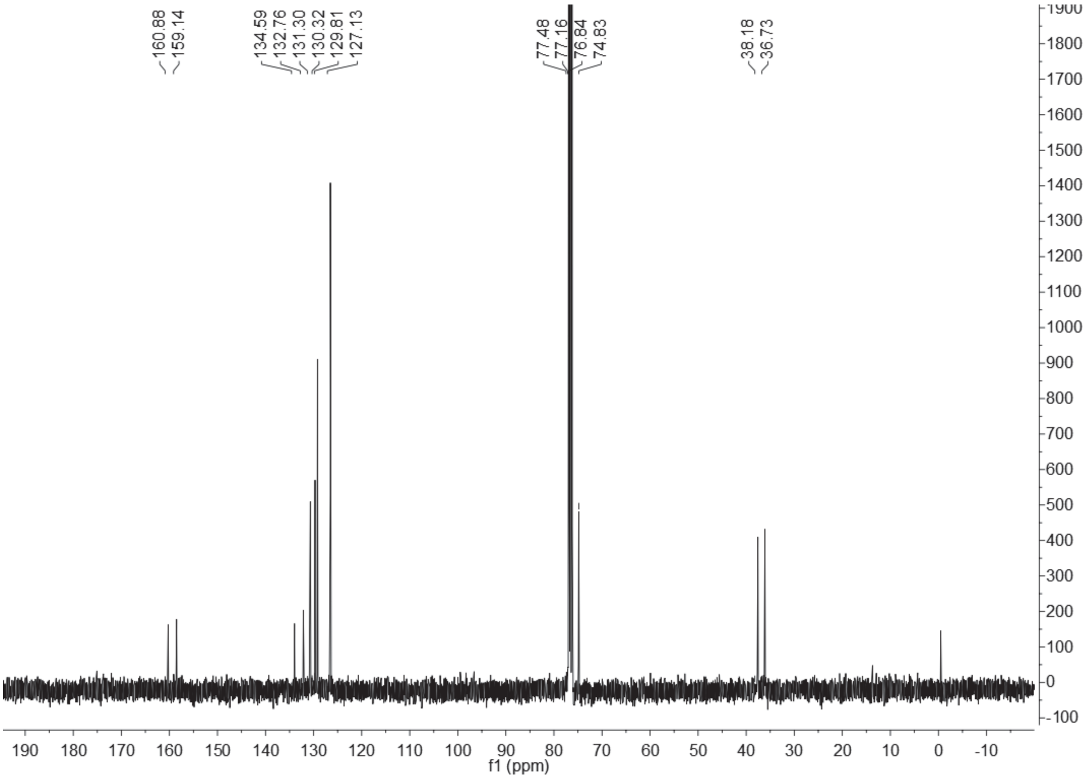
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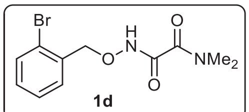
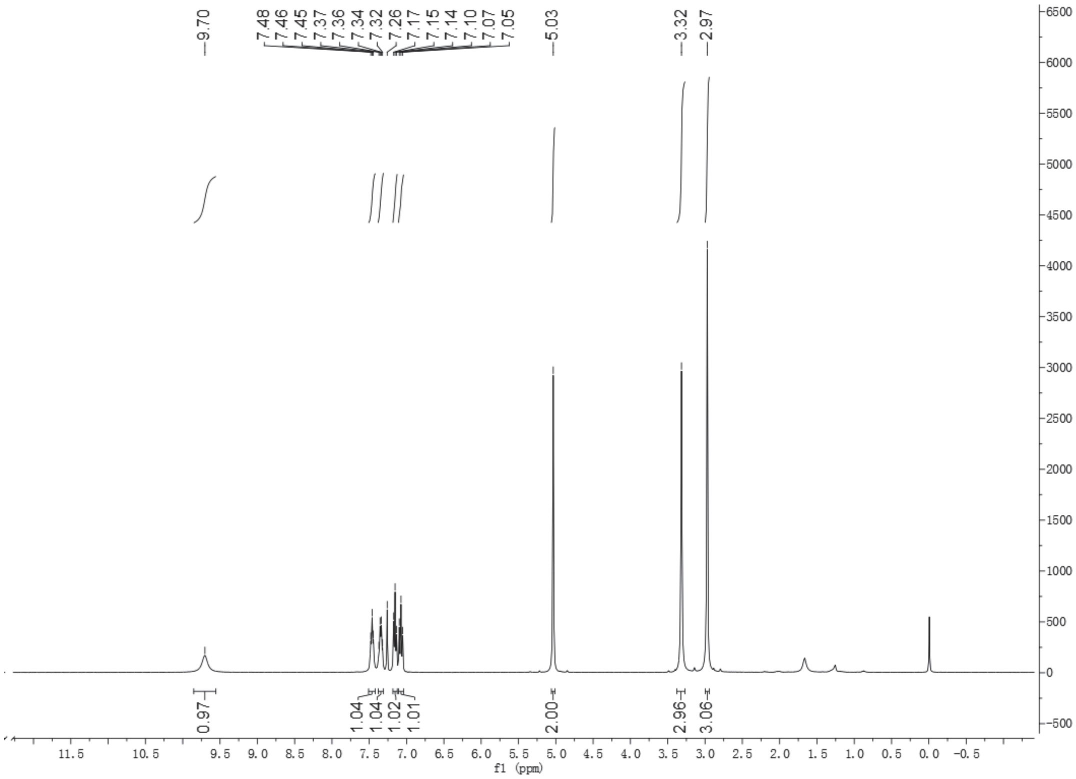
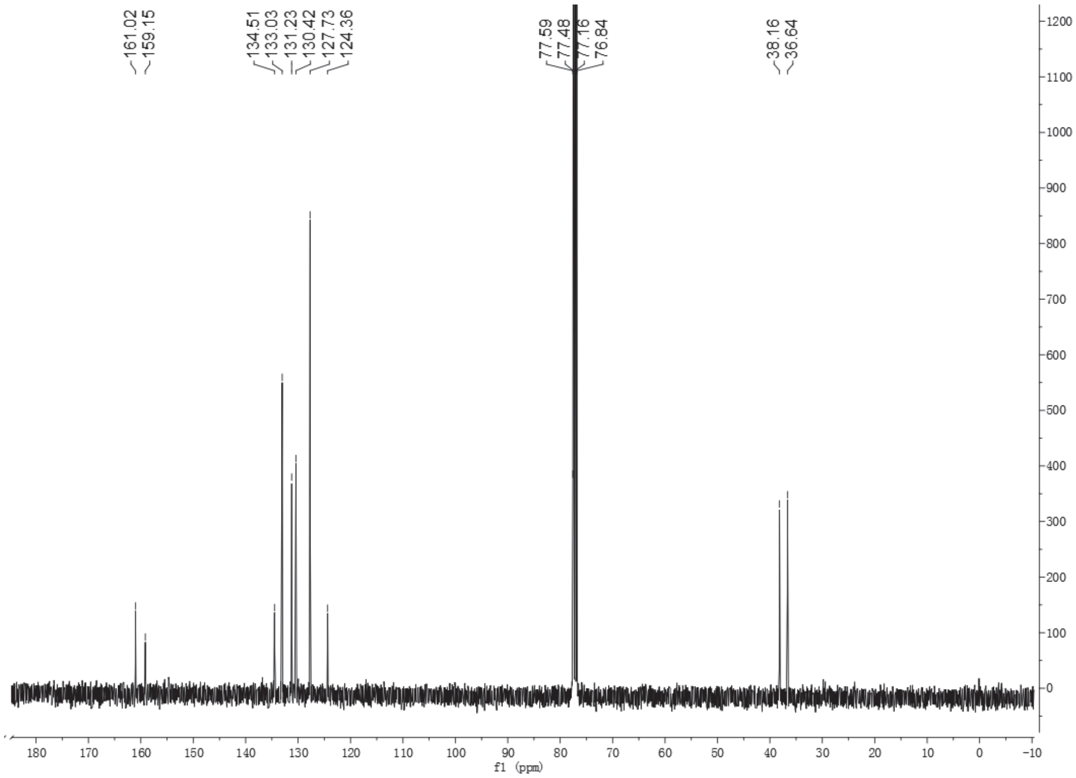
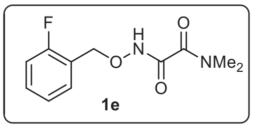
20
10
0
-10
f1 (ppm)


Br
H
N
O
O
O
NMe2

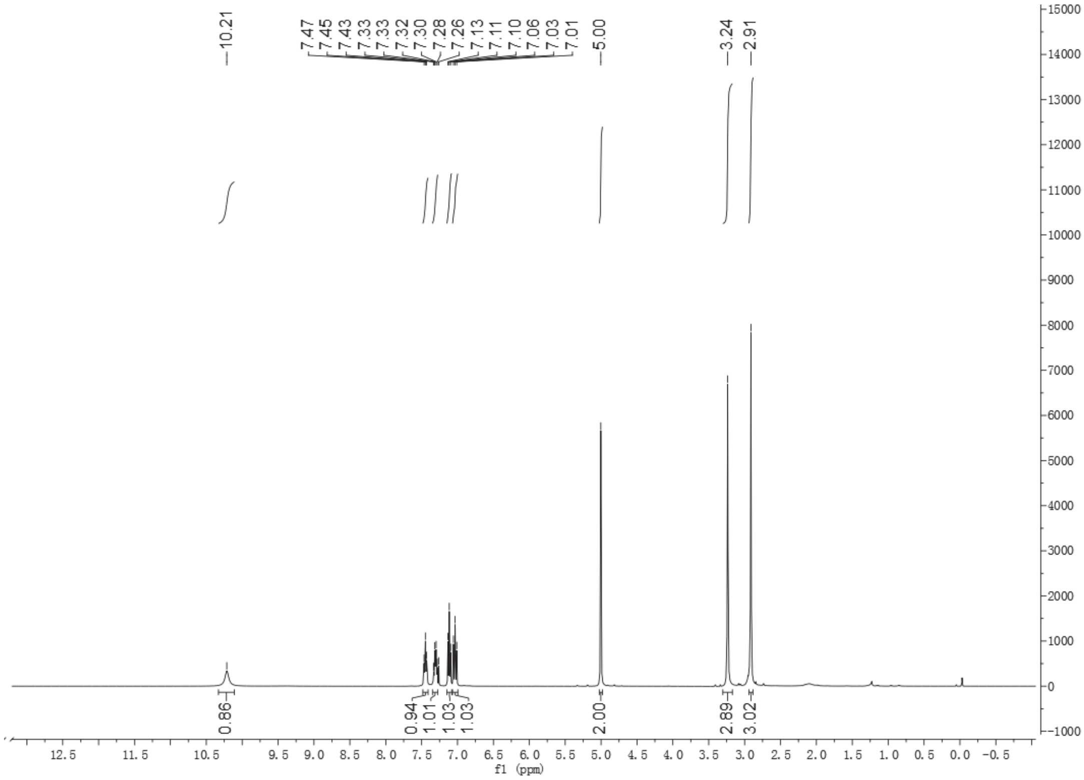
1d

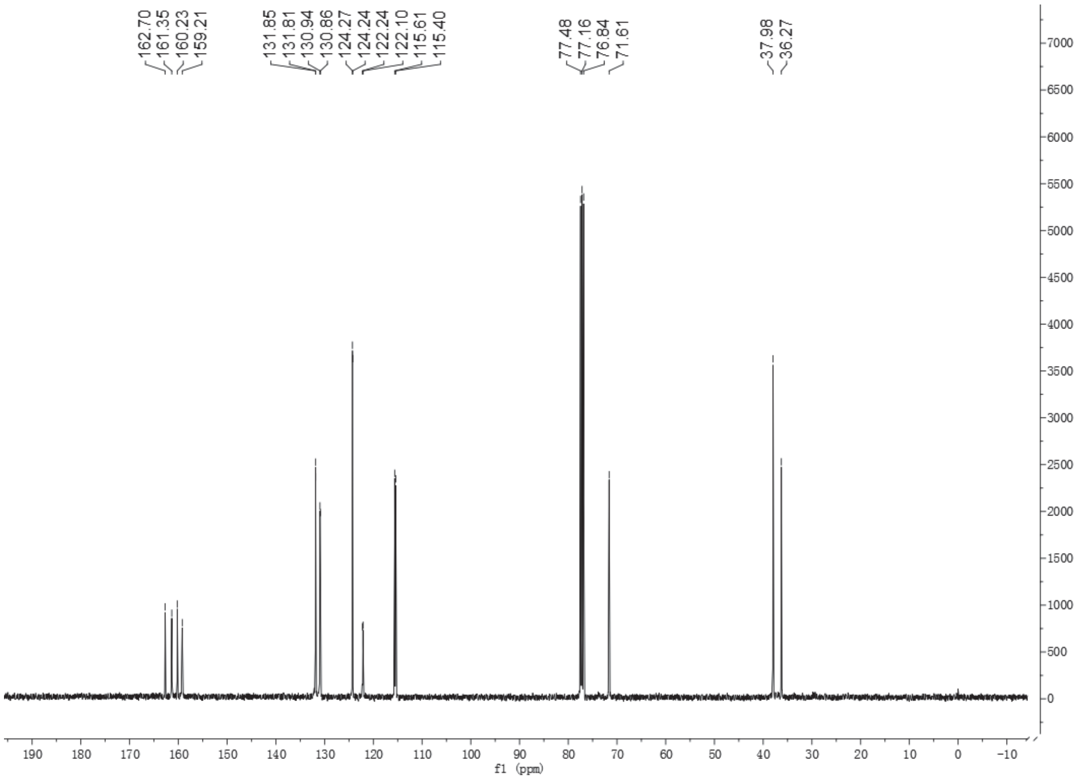

9.70
7.48
7.46
7.45
7.37
7.36
7.34
7.32
7.26
7.17
7.15
7.14
7.10
7.07
7.05
5.03
3.32
2.97
0.97
1.04
1.04
1.02
1.01
2.00
2.96
3.06
f1 (ppm)
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

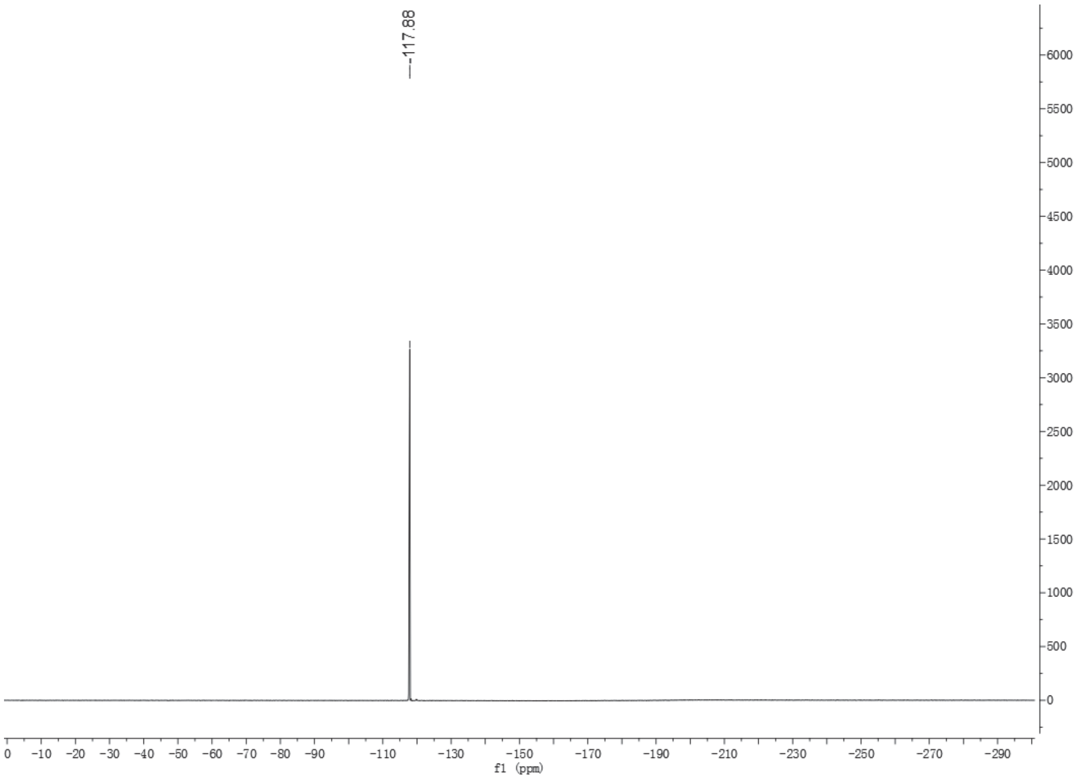

161.02
159.15
134.51
133.03
131.23
130.42
127.73
124.36
77.59
77.48
77.16
76.84
38.16
36.64
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
1200
1100
1000
900
800
700
600
500
400
300
200
100
0

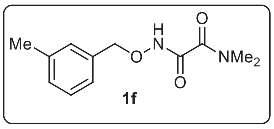

F
H
N
O
O
O
NMe$_2$

1e

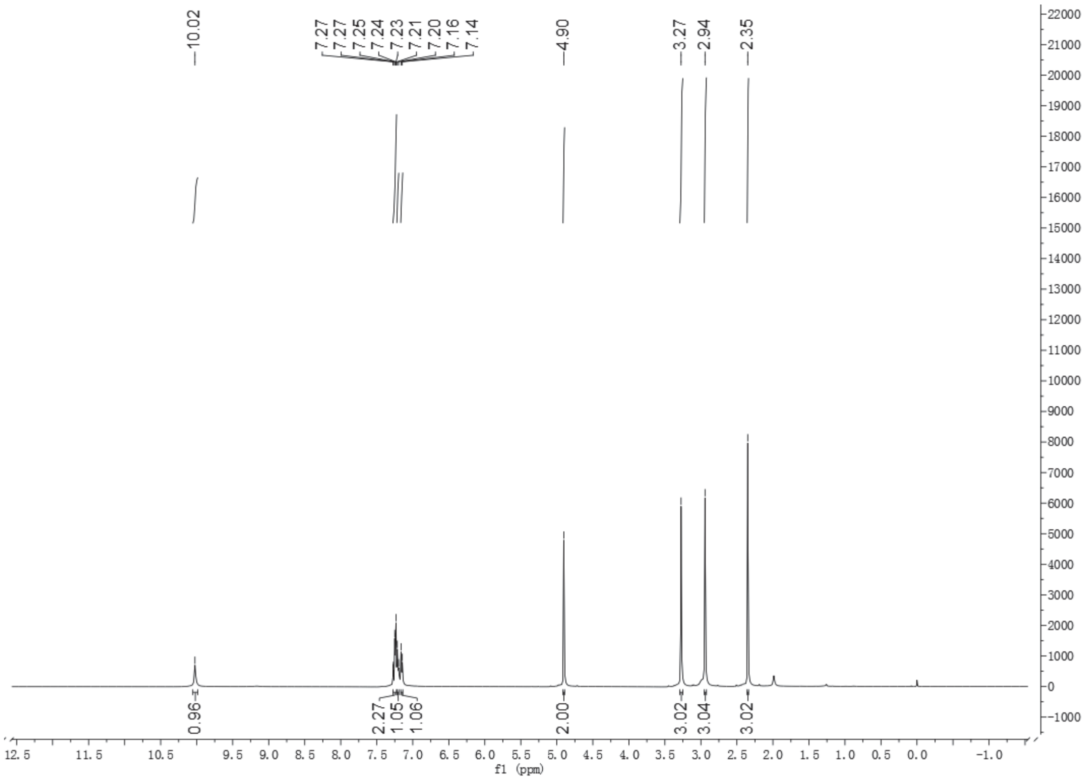

10.21
7.47
7.45
7.43
7.33
7.33
7.32
7.30
7.28
7.26
7.13
7.11
7.10
7.06
7.03
7.01
5.00
3.24
2.91
0.86
0.94
1.01
1.03
1.03
2.00
2.89
3.02
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

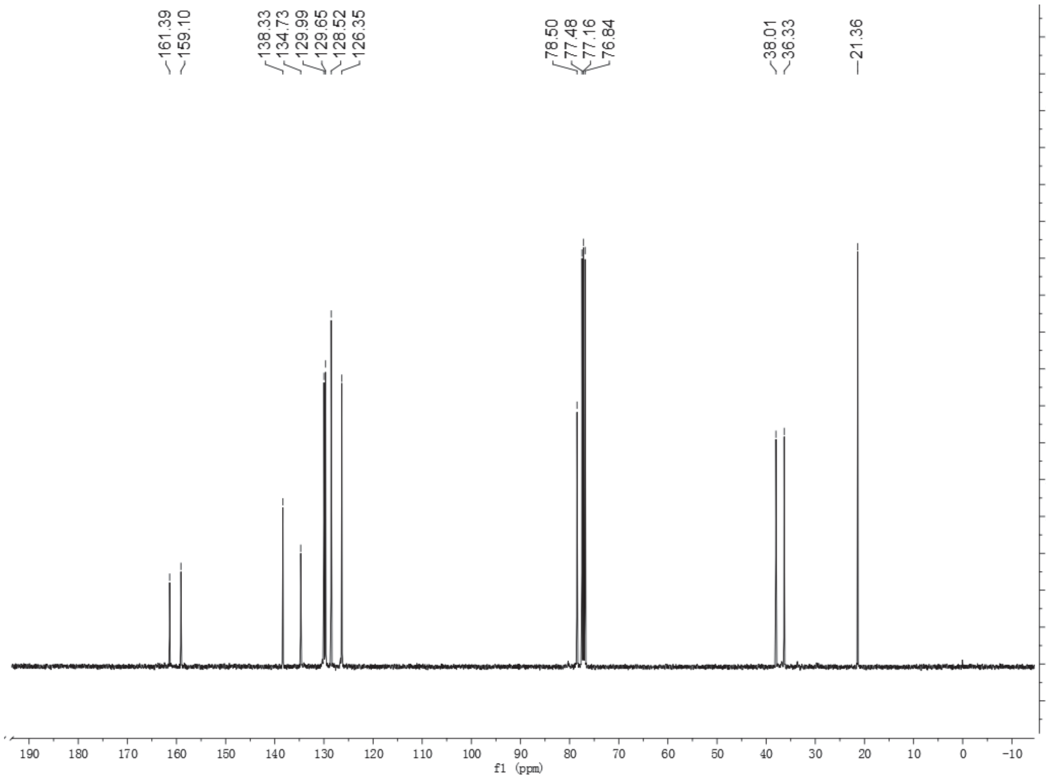

162.70
161.35
160.23
159.21
131.85
131.81
130.94
130.86
124.27
124.24
122.24
122.10
115.61
115.40
77.48
77.16
76.84
71.61
37.98
36.27
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0

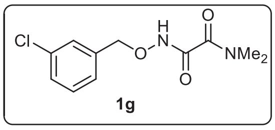

-117.88
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270 -290
f1 (ppm)


Me
H
N
O
O
O
NMe$_2$

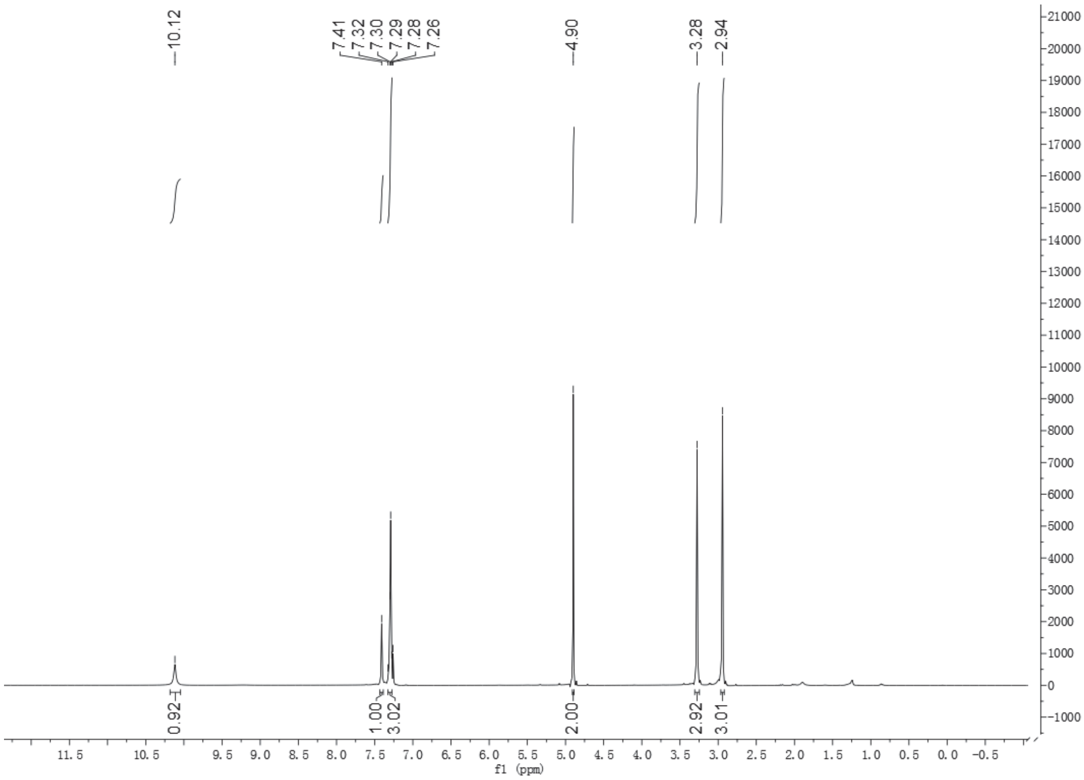
1f

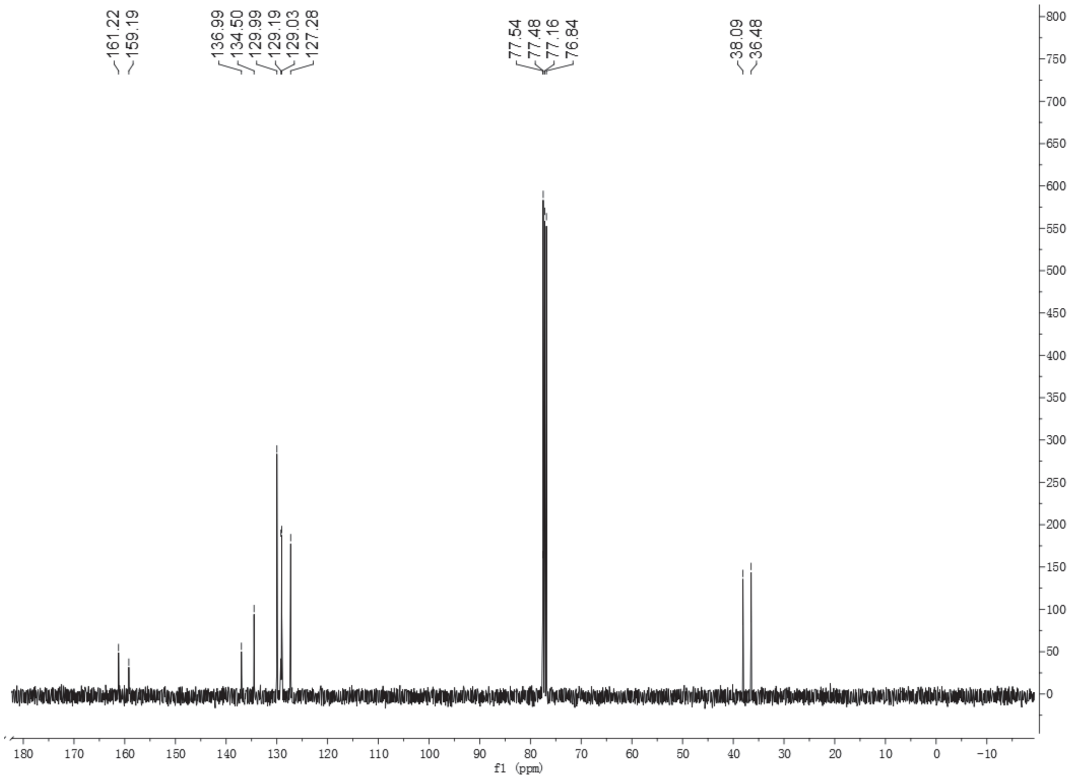

10.02
7.27
7.27
7.25
7.24
7.23
7.21
7.20
7.16
7.14
4.90
3.27
2.94
2.35
0.96
2.27
1.05
1.06
2.00
3.02
3.04
3.02
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -1.0
f1 (ppm)

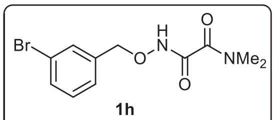

161.39
159.10
138.33
134.73
129.99
129.65
128.52
126.35
78.50
77.48
77.16
76.84
38.01
36.33
21.36
f1 (ppm)


Cl
H
N
O
NMe$_2$

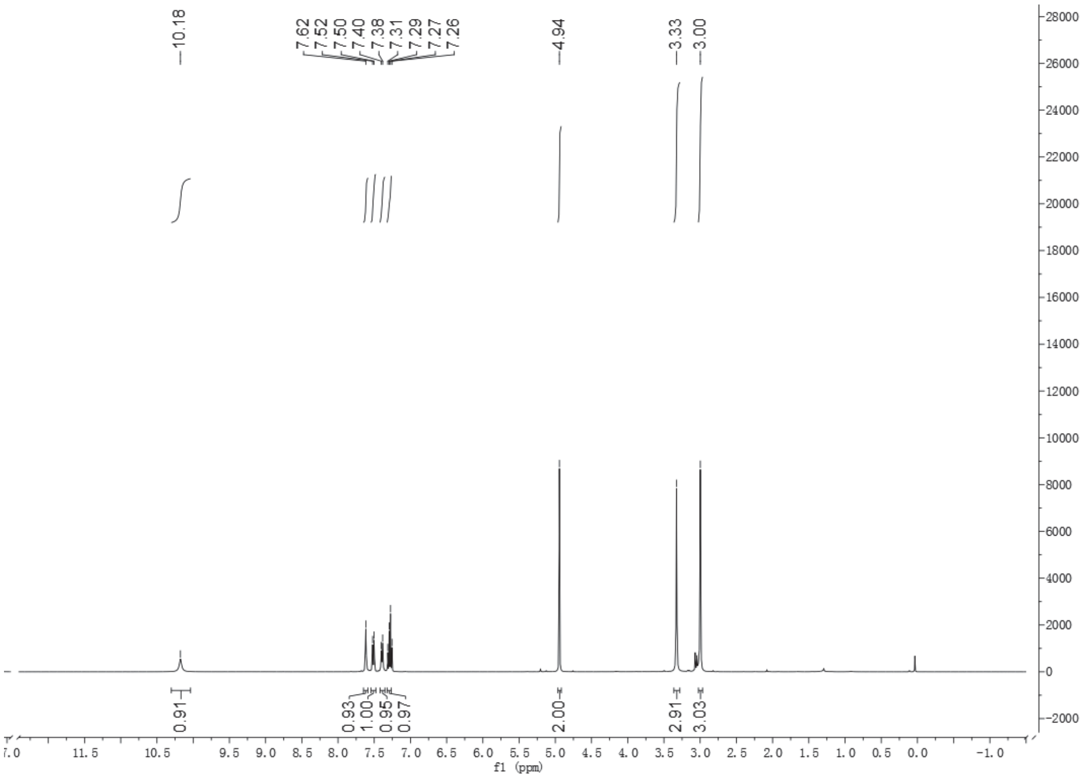
1g

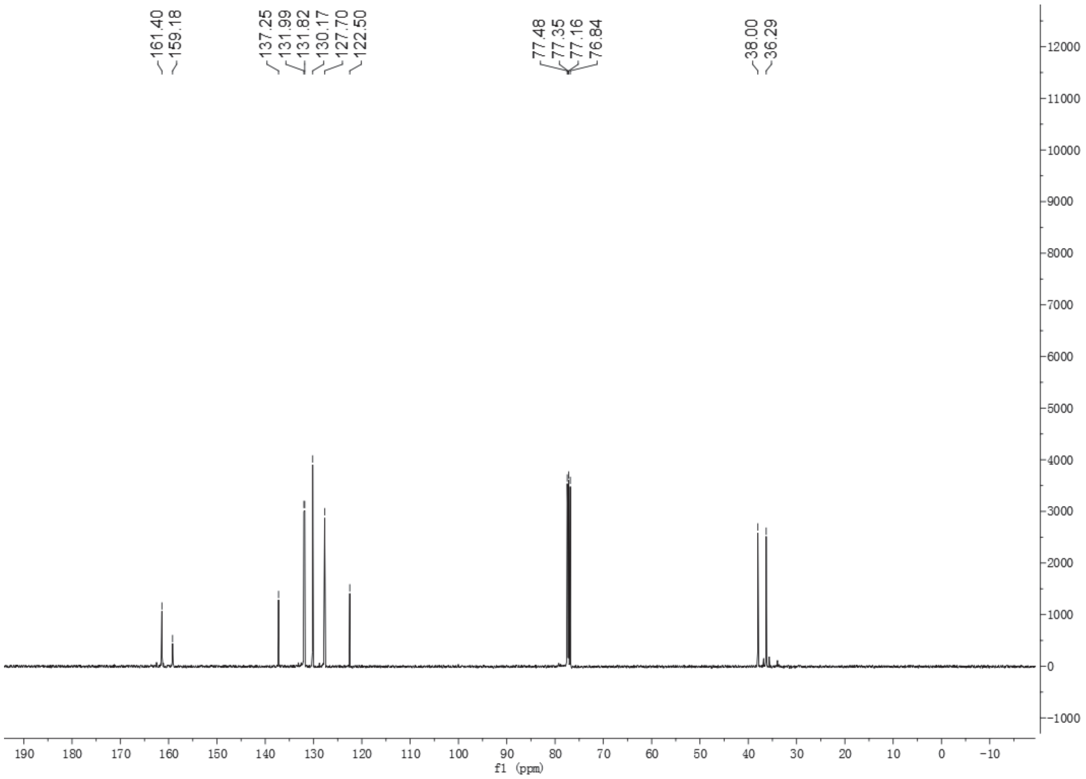

10.12
7.41
7.32
7.30
7.29
7.28
7.26
4.90
3.28
2.94
0.92
1.00
3.02
2.00
2.92
3.01
f1 (ppm)

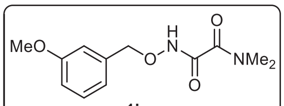

161.22
159.19
136.99
134.50
129.99
129.19
129.03
127.28
77.54
77.48
77.16
76.84
38.09
36.48
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


Br
O
H
N
O
NMe2
O

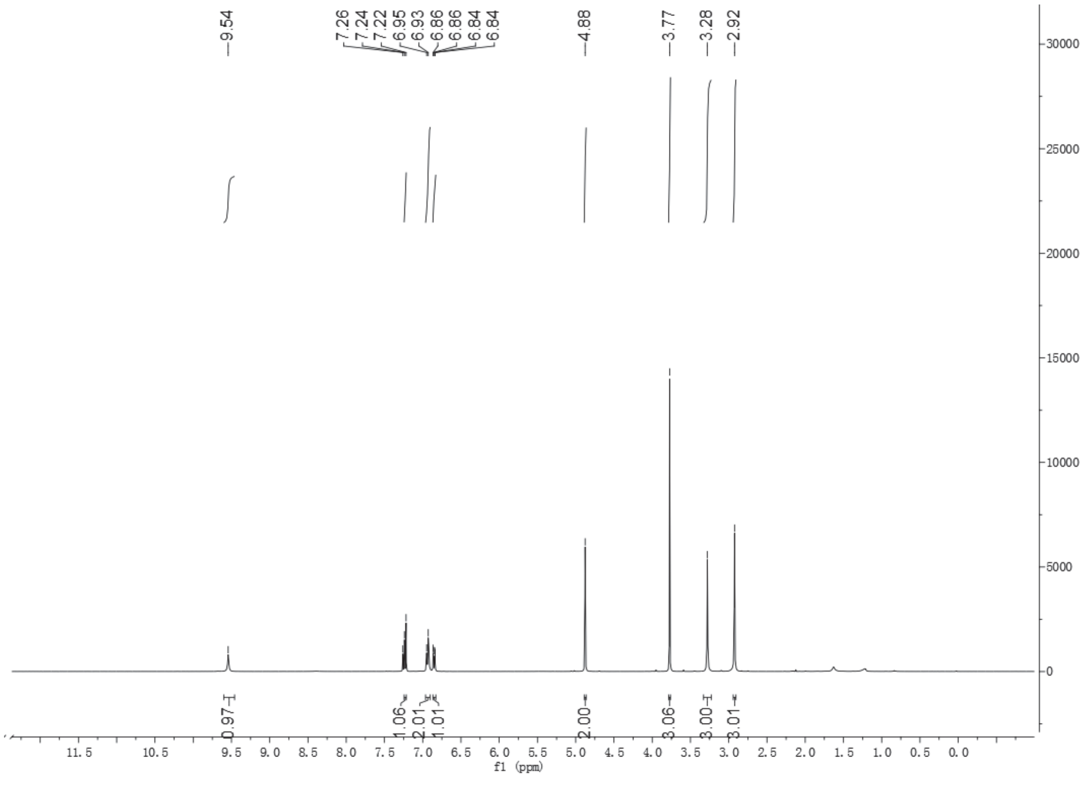
1h

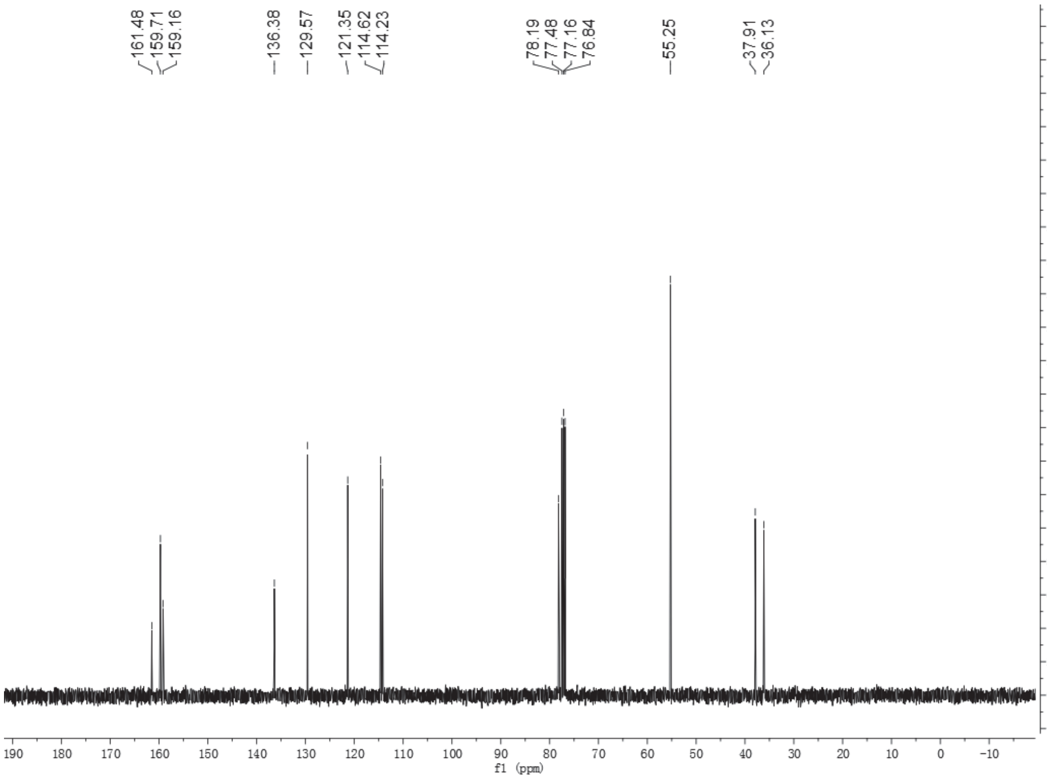

10.18
7.62
7.52
7.50
7.40
7.38
7.31
7.29
7.27
7.26
4.94
3.33
3.00
0.91
0.93
1.00
0.95
0.97
2.00
2.91
3.03
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
−2000
7.0 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −1.0
f1 (ppm)

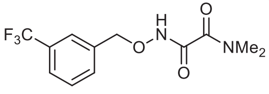

161.40
159.18
137.25
131.99
131.82
130.17
127.70
122.50
77.48
77.35
77.16
76.84
38.00
36.29
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


MeO
H
N
O
O
O
NMe2

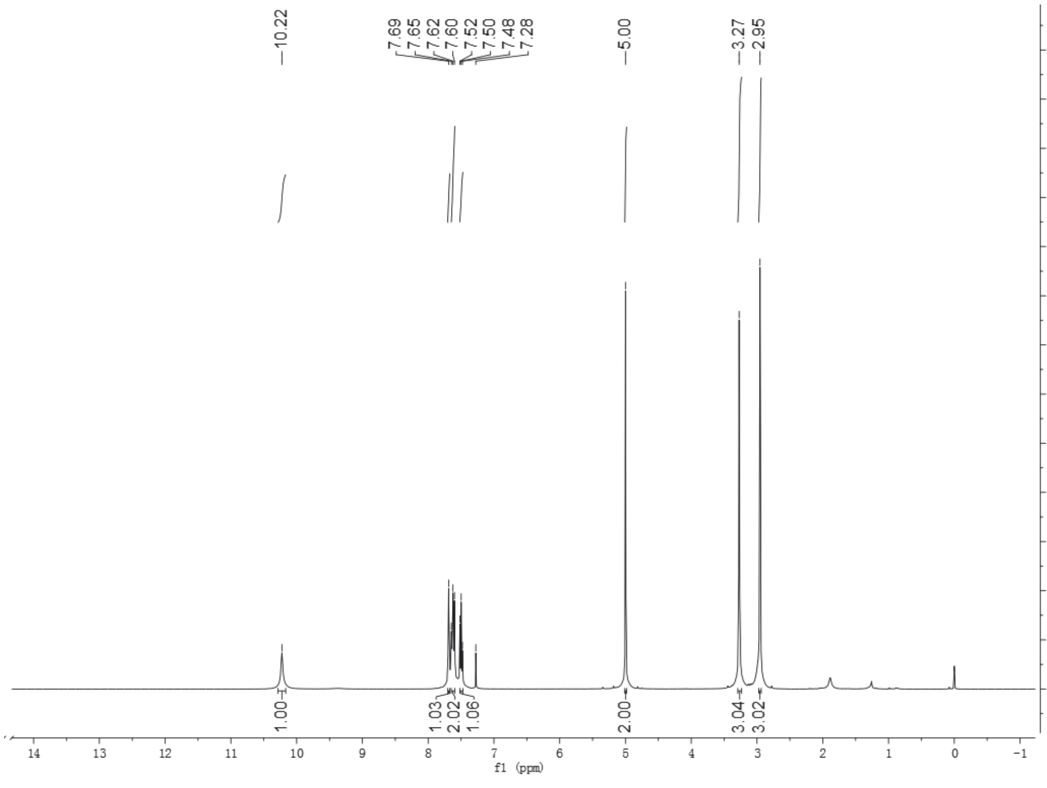
1i

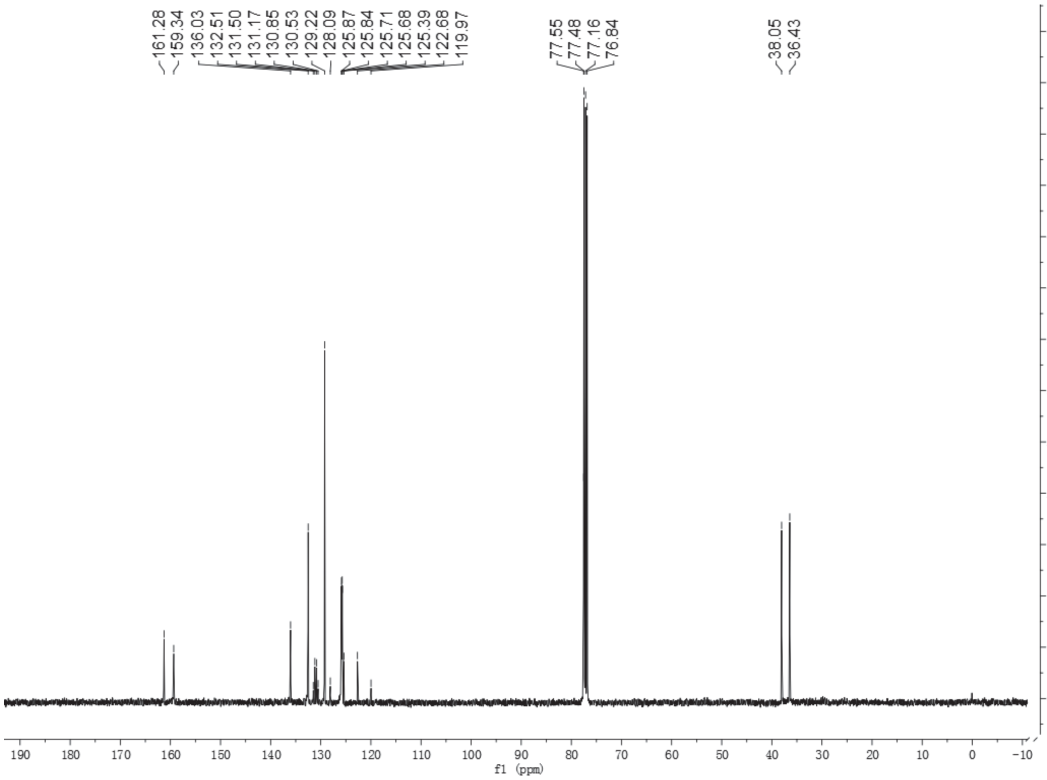

9.54
7.26
7.24
7.22
6.95
6.93
6.86
6.86
6.84
6.84
4.88
3.77
3.28
2.92
30000
25000
20000
15000
10000
5000
0
0.97
1.06
2.01
1.01
2.00
3.06
3.00
3.01
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

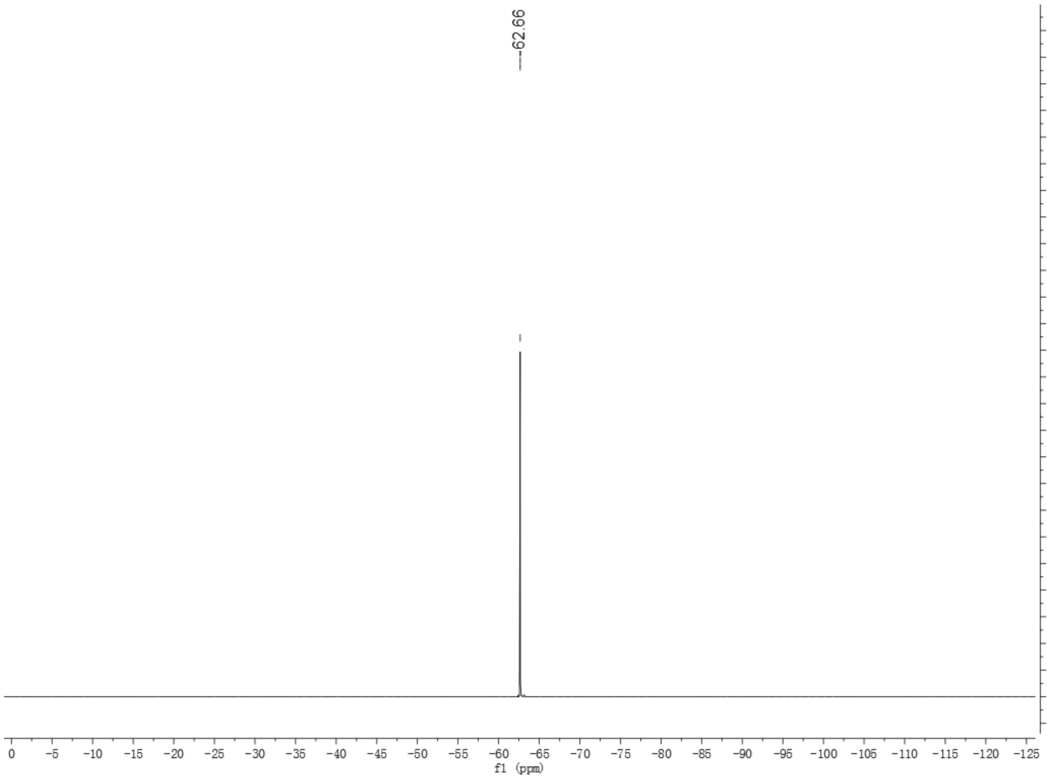

161.48
159.71
159.16
136.38
129.57
121.35
114.62
114.23
78.19
77.48
77.16
76.84
55.25
37.91
36.13
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)
400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20 0 −20

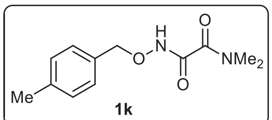

F$_3$C
O
H
N
O
O
NMe$_2$

1j


10.22
7.69
7.65
7.62
7.60
7.52
7.50
7.48
7.28
5.00
3.27
2.95
1.00
1.03
2.02
1.06
2.00
3.04
3.02
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)
6500 6000 5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0

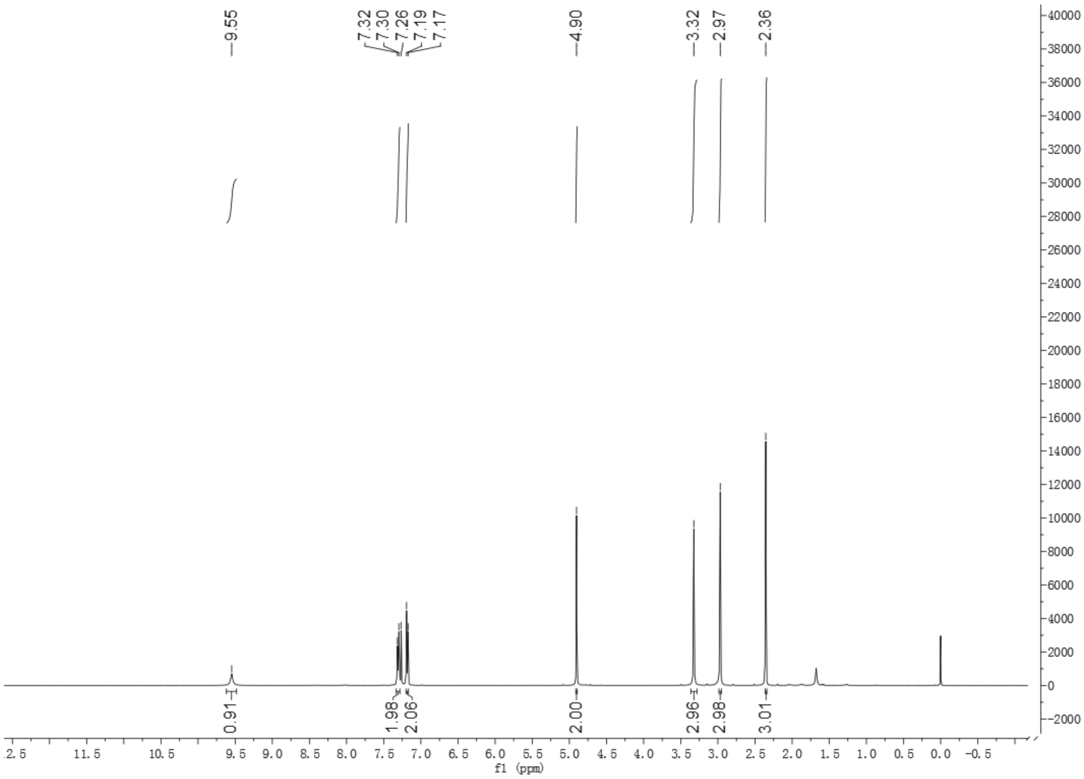

161.28
159.34
136.03
132.51
131.50
131.17
130.85
130.53
129.22
128.09
125.87
125.84
125.71
125.68
125.39
122.68
119.97
77.55
77.48
77.16
76.84
38.05
36.43
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)
6500 6000 5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0


−62.66
0 −5 −10 −15 −20 −25 −30 −35 −40 −45 −50 −55 −60 −65 −70 −75 −80 −85 −90 −95 −100 −105 −110 −115 −120 −125
f1 (ppm)
25000 24000 23000 22000 21000 20000 19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000

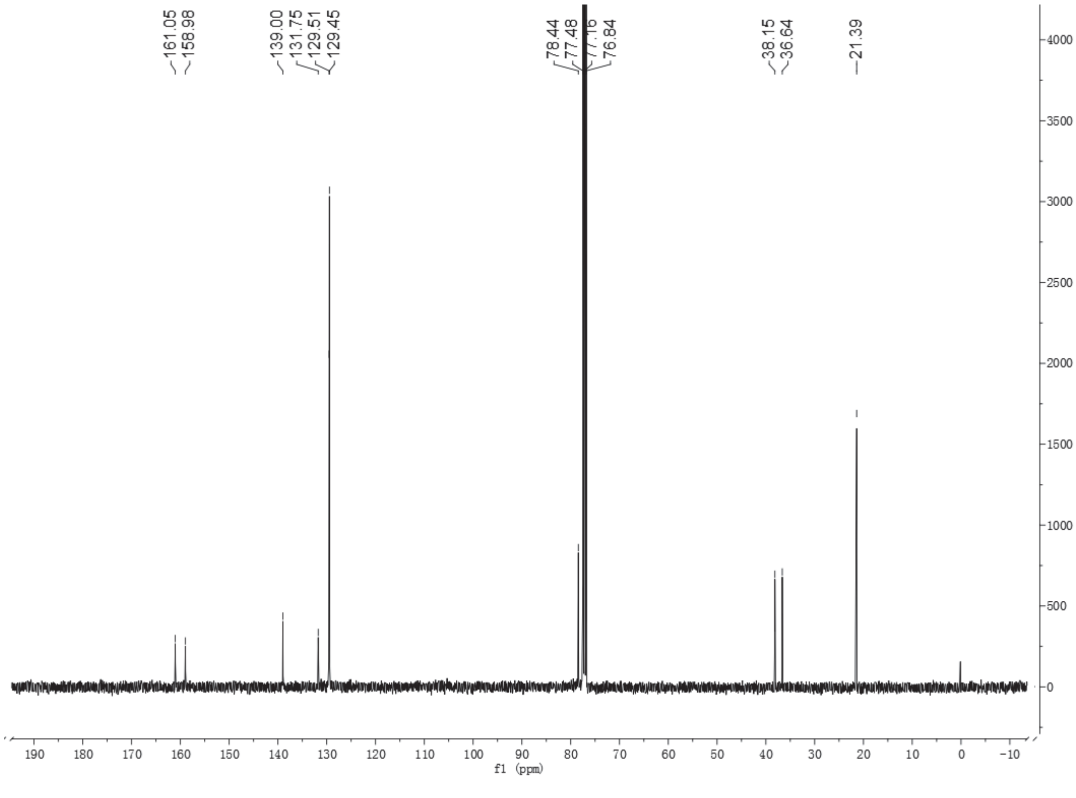


Me
H
N
O
O
O
NMe$_2$

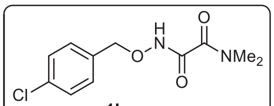
1k



9.55
7.32
7.30
7.26
7.19
7.17
4.90
3.32
2.97
2.36
0.91
1.98
2.06
2.00
2.96
2.98
3.01
f1 (ppm)

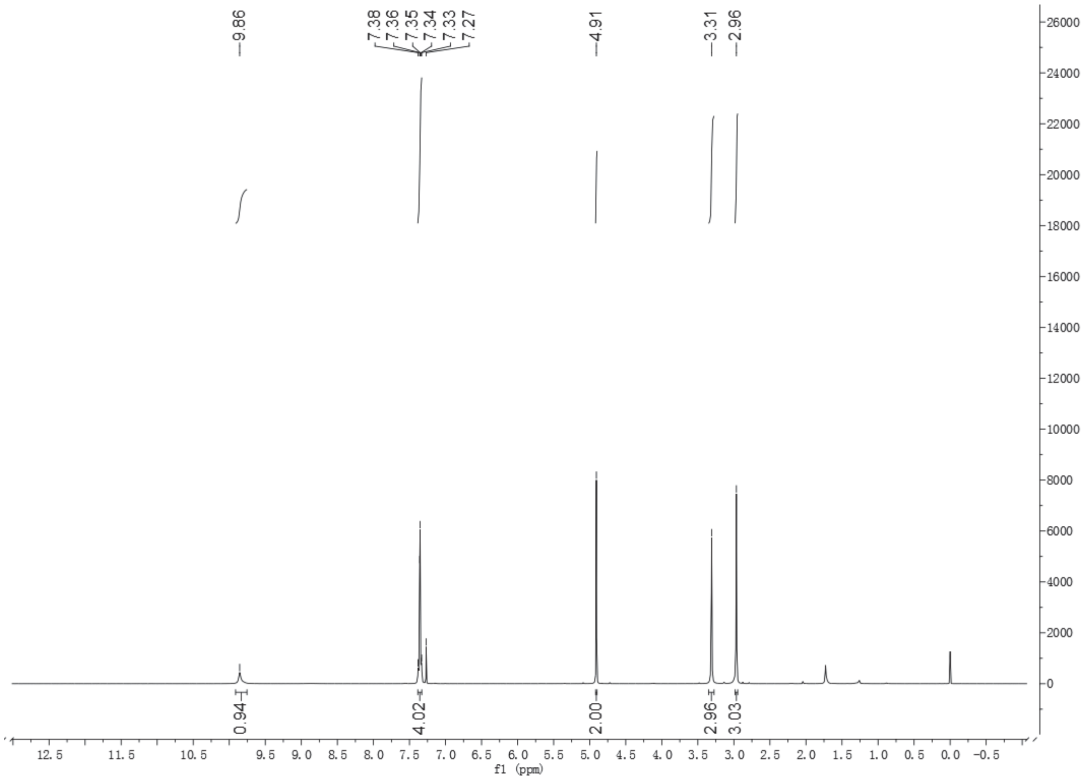


161.05
158.98
139.00
131.75
129.51
129.45
78.44
77.48
77.16
76.84
38.15
36.64
21.39
f1 (ppm)

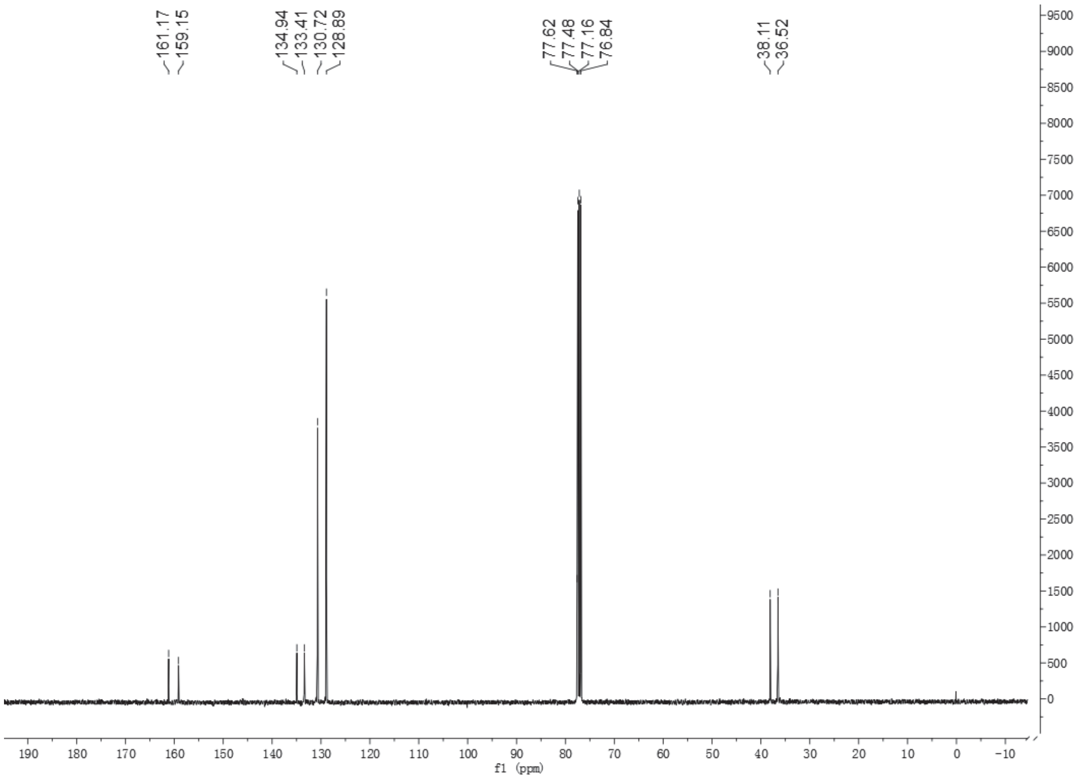


H
N
O
O
O
NMe$_2$
Cl

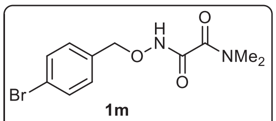
1l



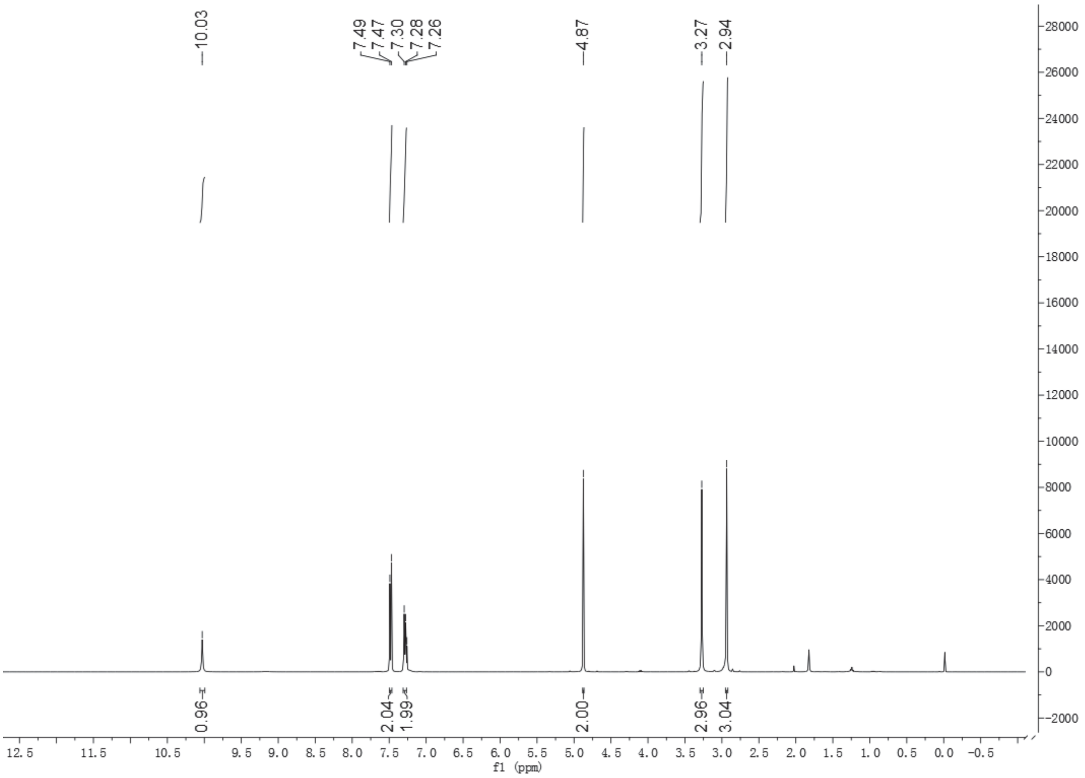
9.86
7.38
7.36
7.35
7.34
7.33
7.27
4.91
3.31
2.96
0.94
4.02
2.00
2.96
3.03
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0

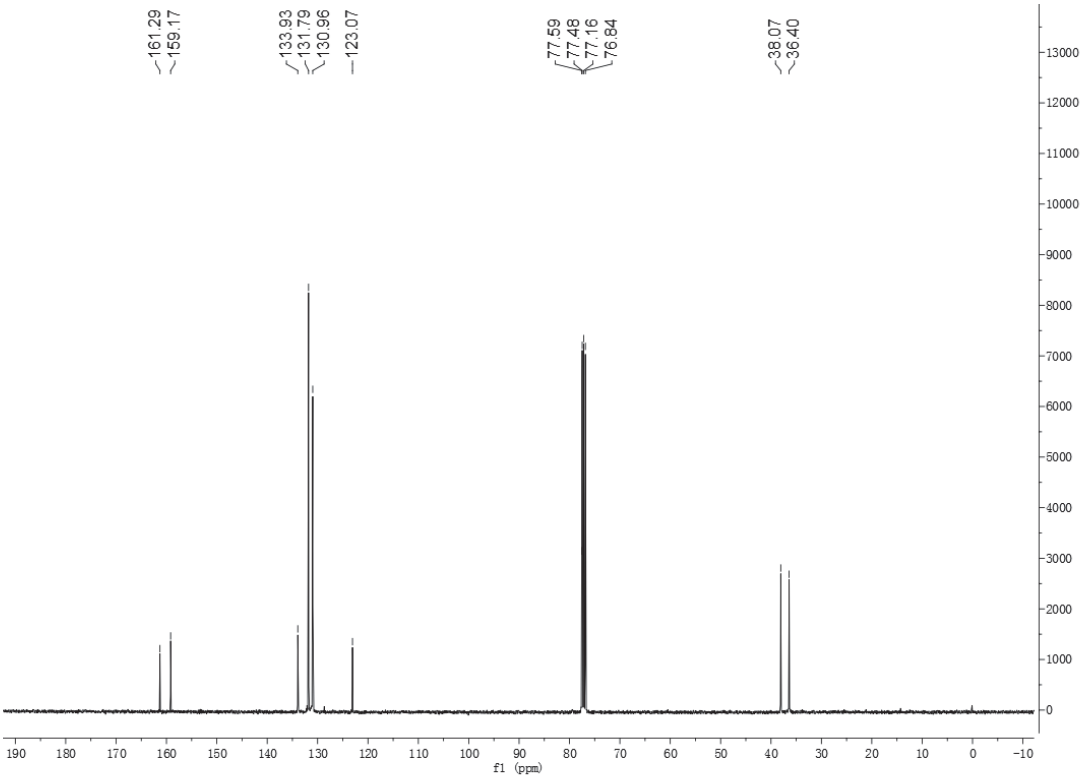


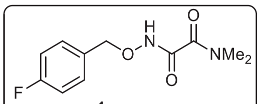
161.17
159.15
134.94
133.41
130.72
128.89
77.62
77.48
77.16
76.84
38.11
36.52
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
9500
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0


H
O
O
NMe$_2$
O
Br

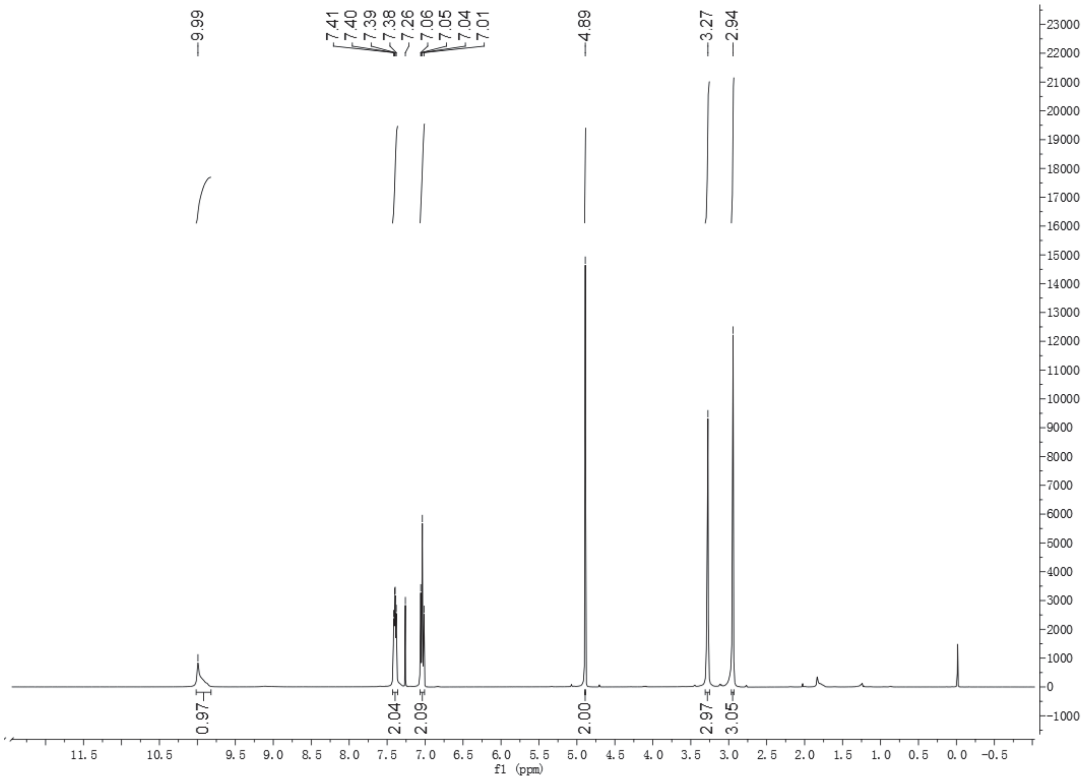
1m

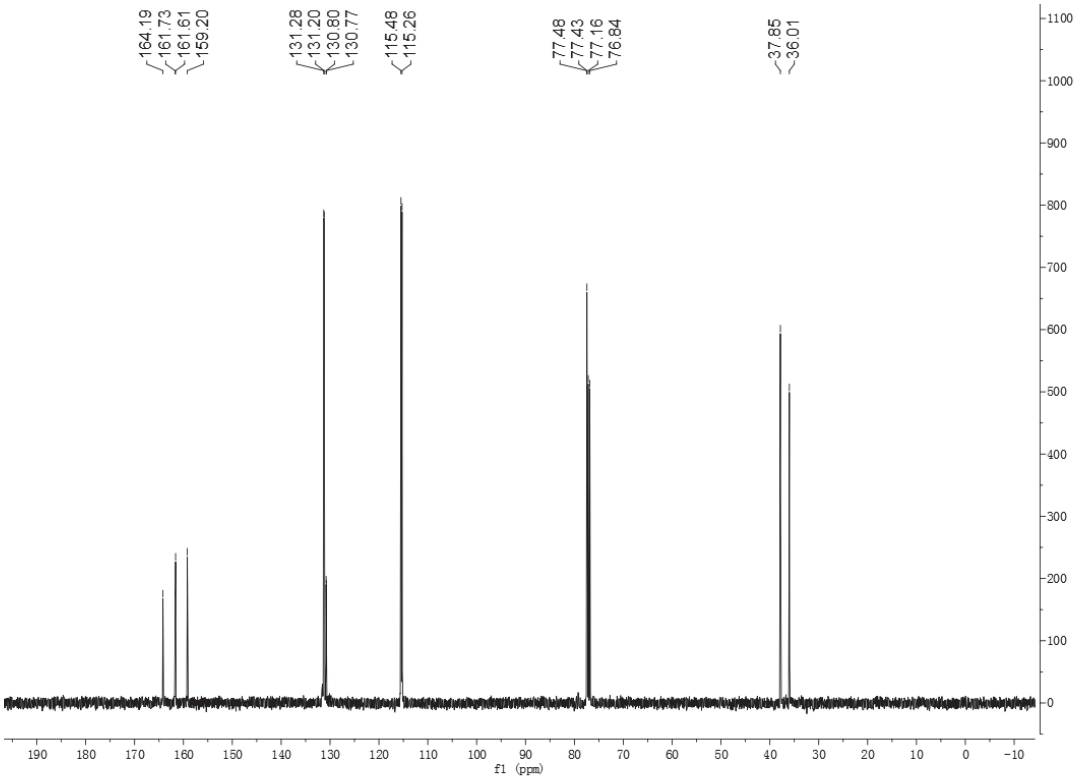

10.03
7.49
7.47
7.30
7.28
7.26
4.87
3.27
2.94
0.96
2.04
1.99
2.00
2.96
3.04
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

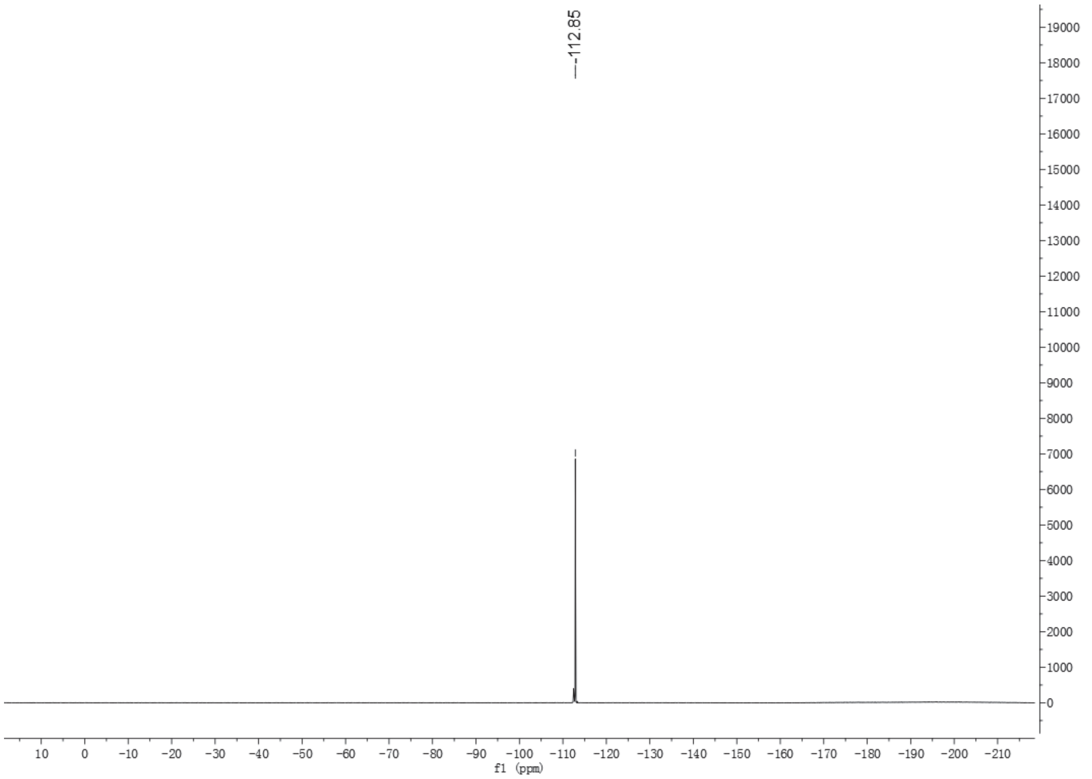

161.29
159.17
133.93
131.79
130.96
123.07
77.59
77.48
77.16
76.84
38.07
36.40
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

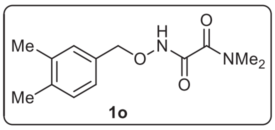

F
H
N
O
O
O
NMe$_2$

1n

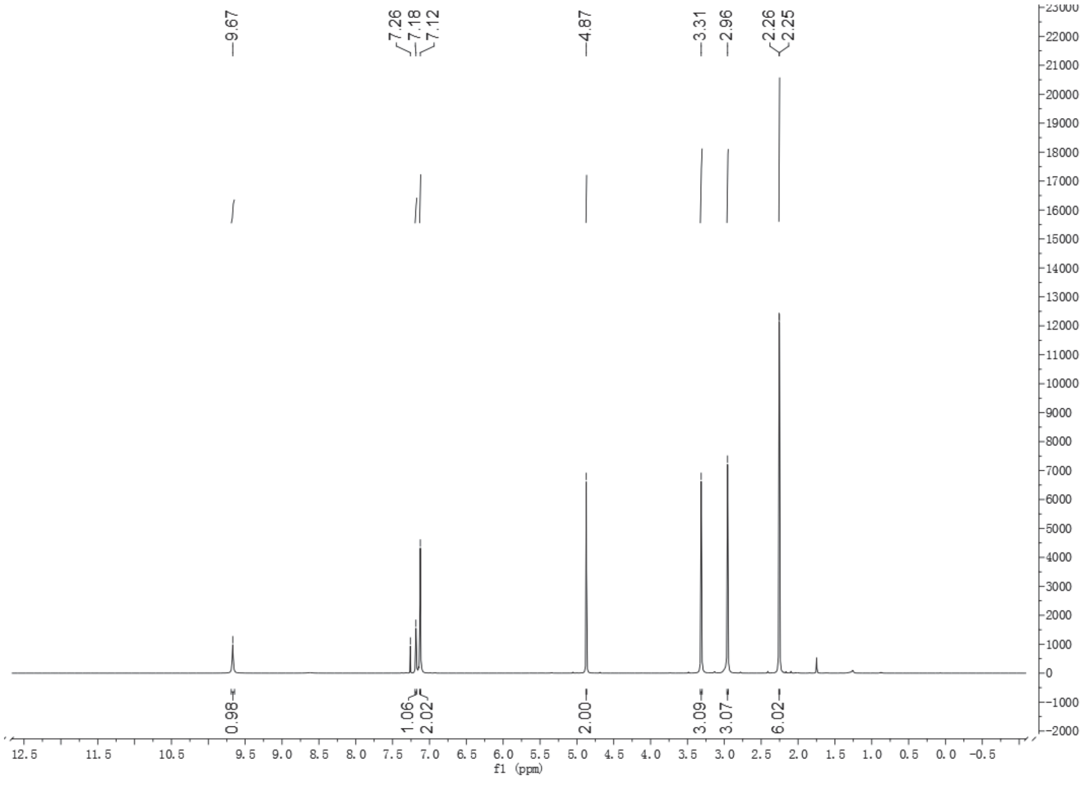

9.99
7.41
7.40
7.39
7.38
7.26
7.06
7.05
7.04
7.01
4.89
3.27
2.94
0.97
2.04
2.09
2.00
2.97
3.05
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

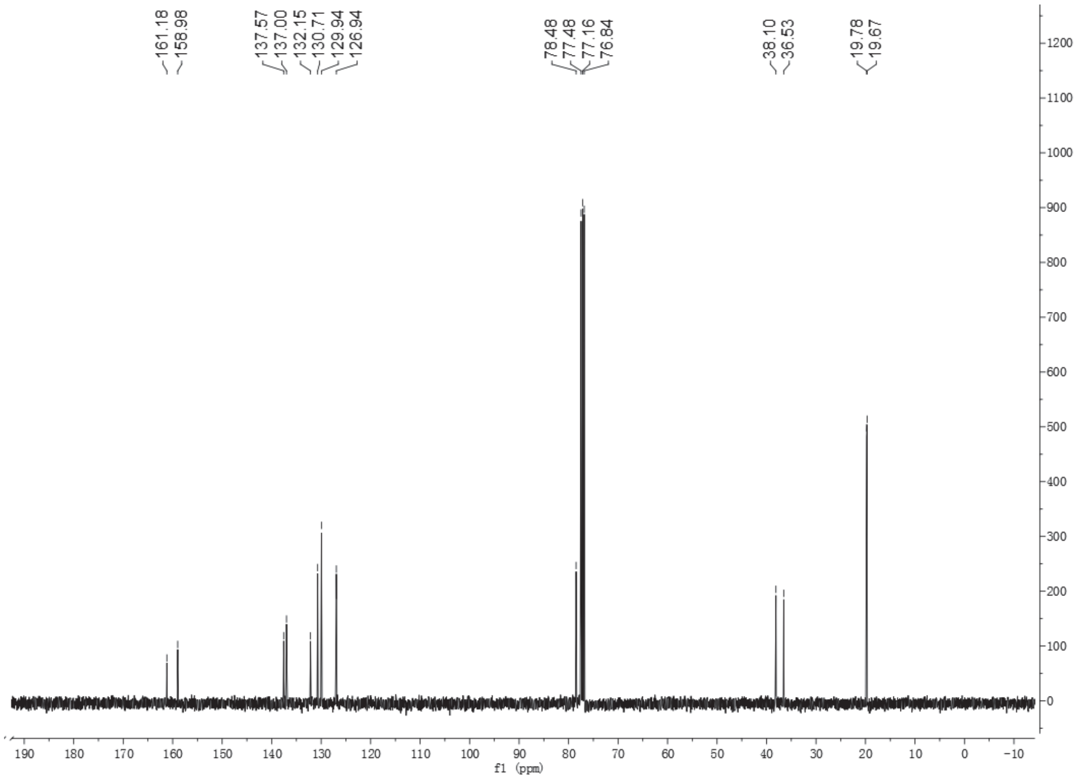

164.19
161.73
161.61
159.20
131.28
131.20
130.80
130.77
115.48
115.26
77.48
77.43
77.16
76.84
37.85
36.01
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1100
1000
900
800
700
600
500
400
300
200
100
0

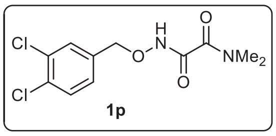

-112.85
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)


Me
Me
O
H
N
O
O
NMe2

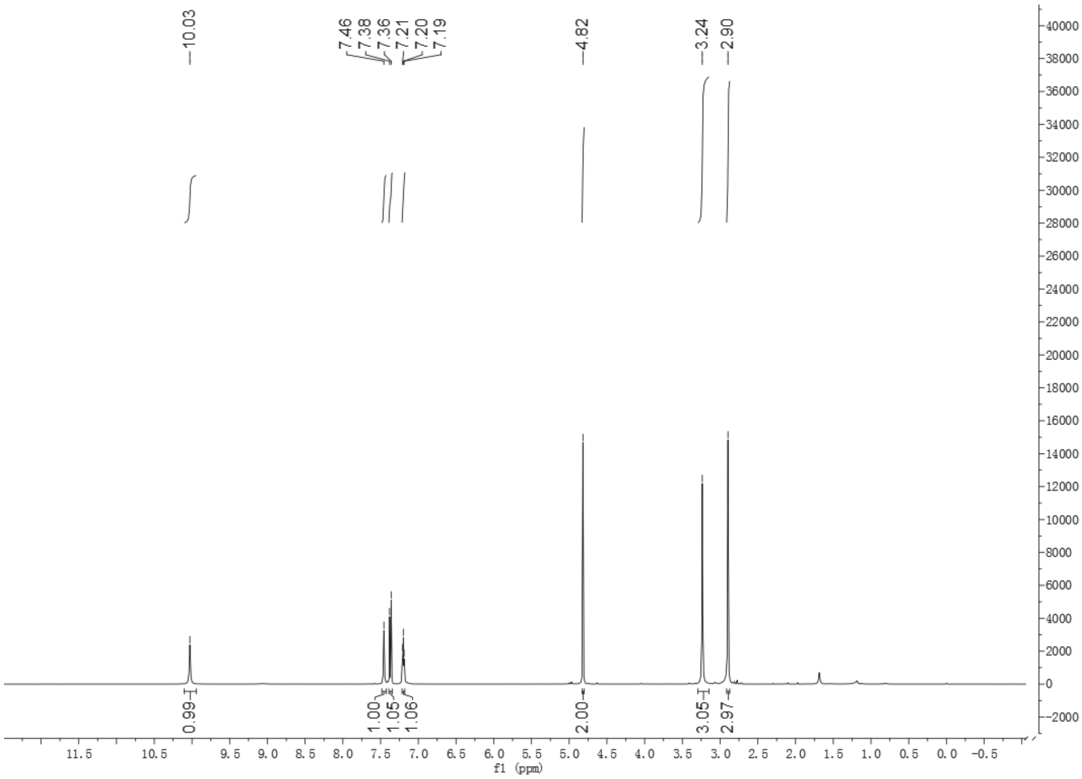
1o

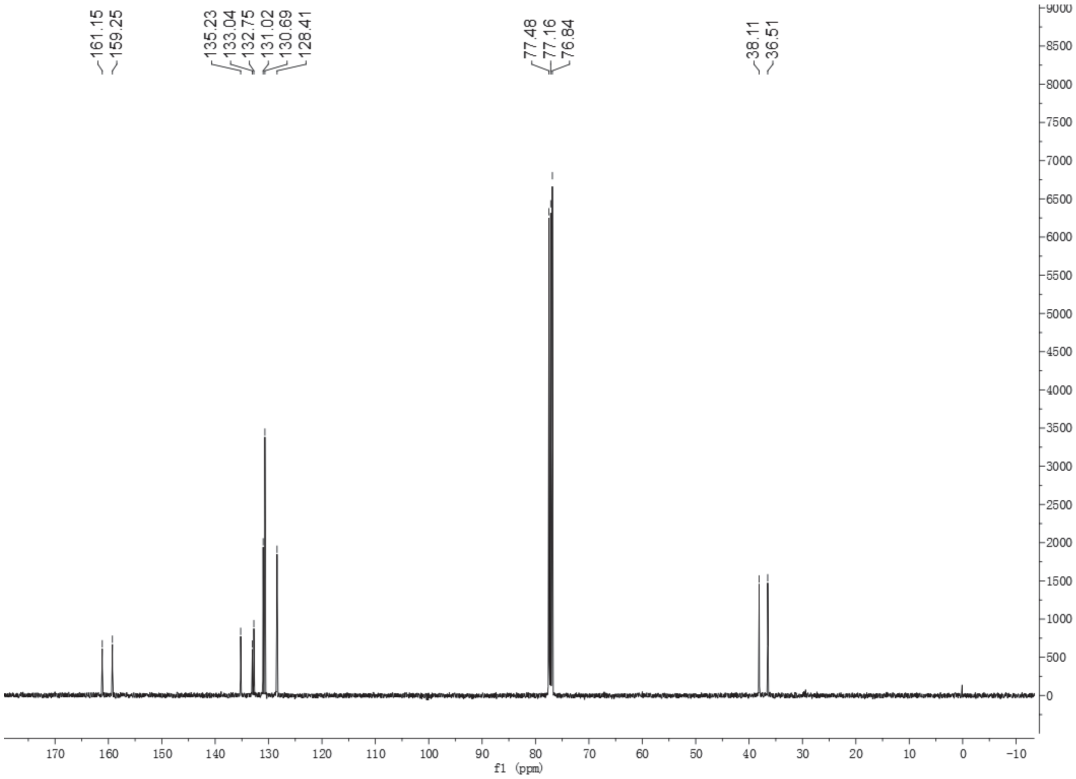

9.67
7.26
7.18
7.12
4.87
3.31
2.96
2.26
2.25
0.98
1.06
2.02
2.00
3.09
3.07
6.02
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
−2000
12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

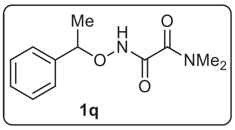

161.18
158.98
137.57
137.00
132.15
130.71
129.94
126.94
78.48
77.48
77.16
76.84
38.10
36.53
19.78
19.67
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
1200 1100 1000 900 800 700 600 500 400 300 200 100 0


Cl
Cl
O
H
N
O
O
NMe2

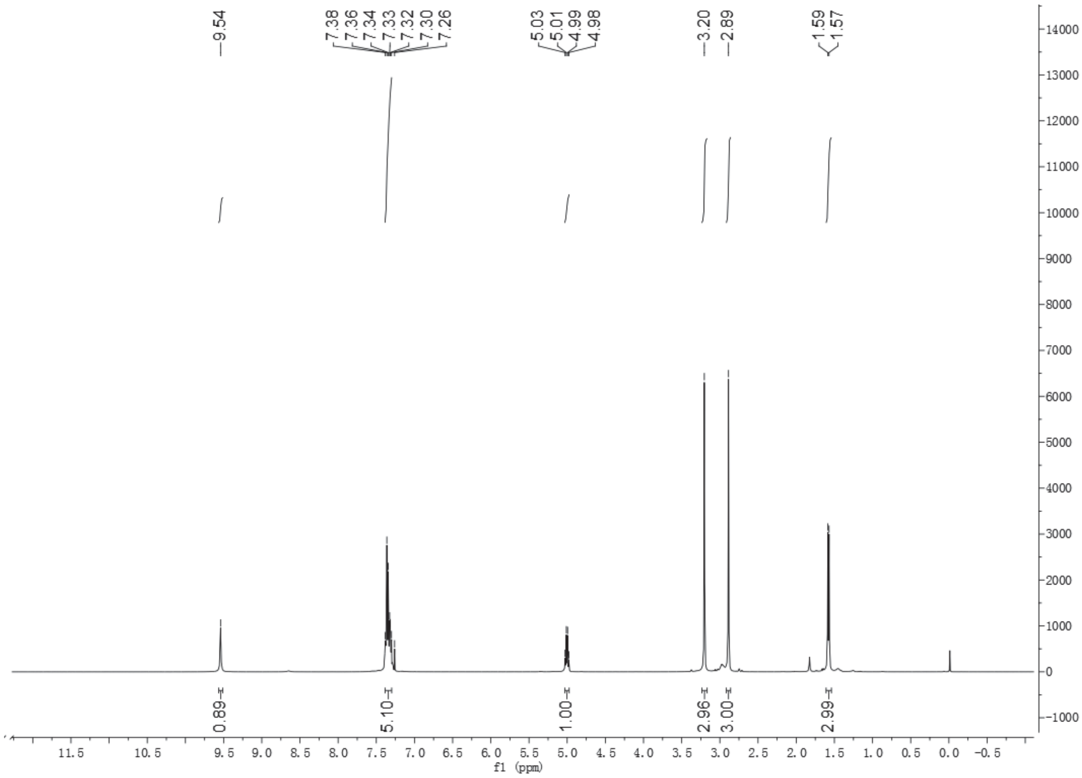
1p

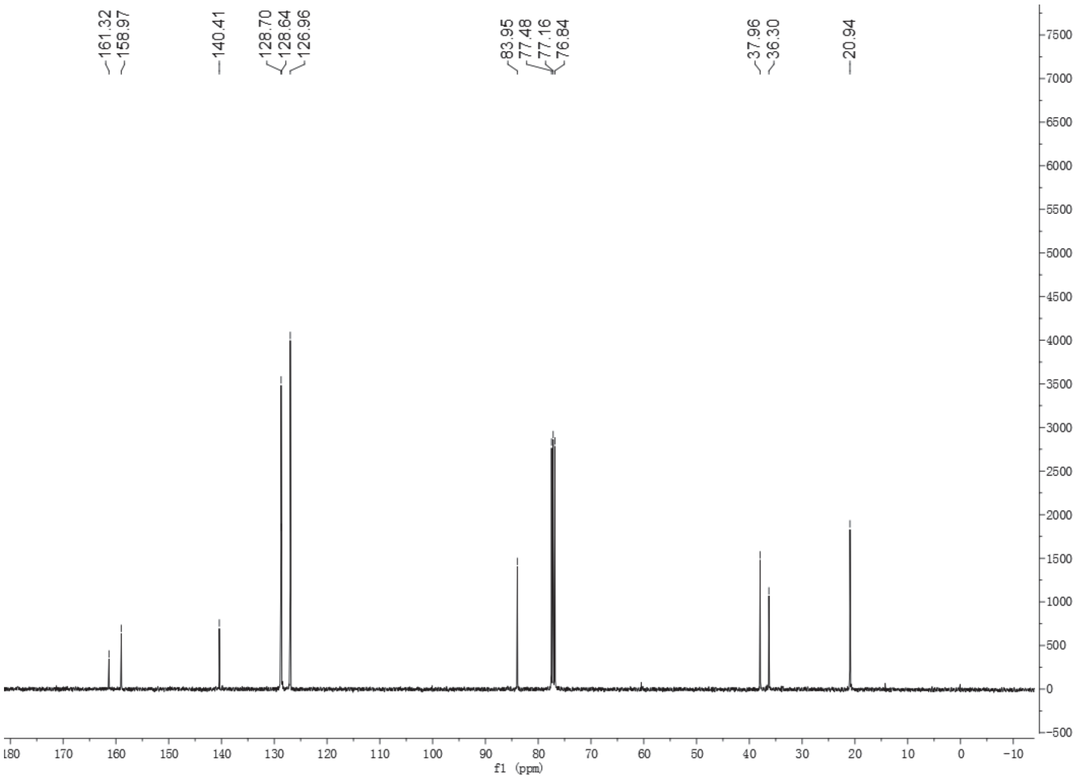

10.03
7.46
7.38
7.36
7.21
7.20
7.19
4.82
3.24
2.90
0.99
1.00
1.05
1.06
2.00
3.05
2.97
f1 (ppm)
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
40000 38000 36000 34000 32000 30000 28000 26000 24000 22000 20000 18000 16000 14000 12000 10000 8000 6000 4000 2000 0 -2000

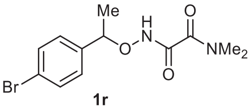

161.15
159.25
135.23
133.04
132.75
131.02
130.69
128.41
77.48
77.16
76.84
38.11
36.51
f1 (ppm)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
9000 8500 8000 7500 7000 6500 6000 5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0


Me
H
N
O
O
O
NMe2

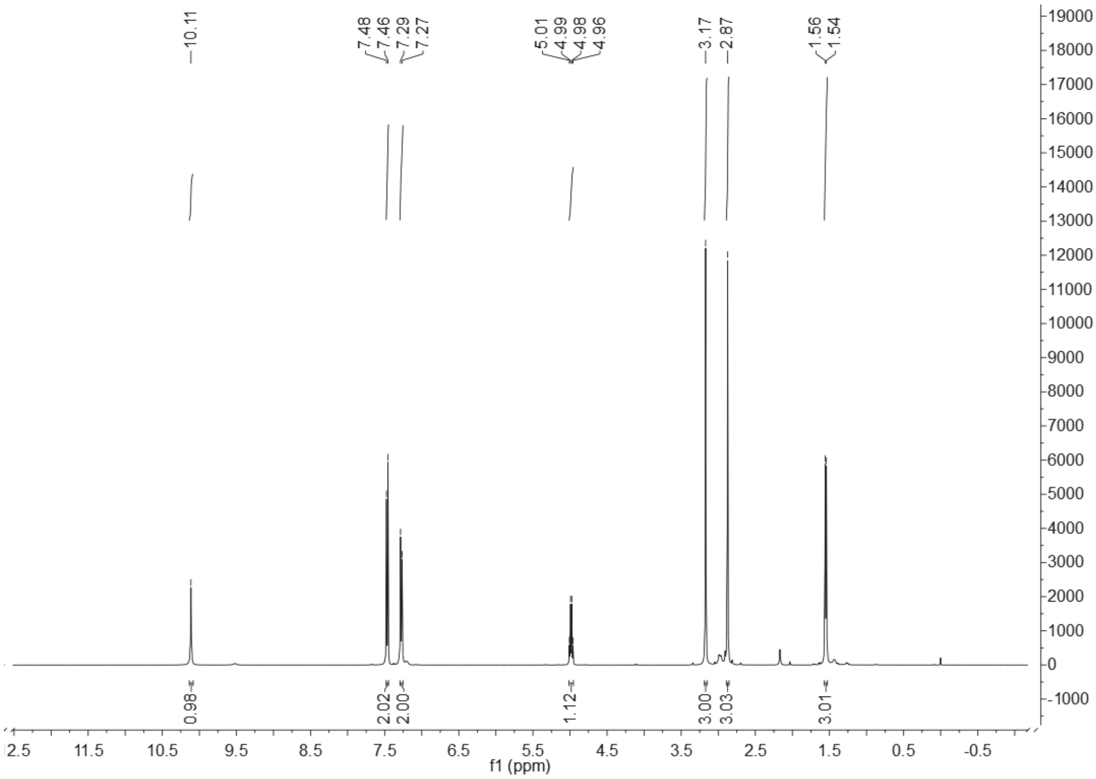
1q

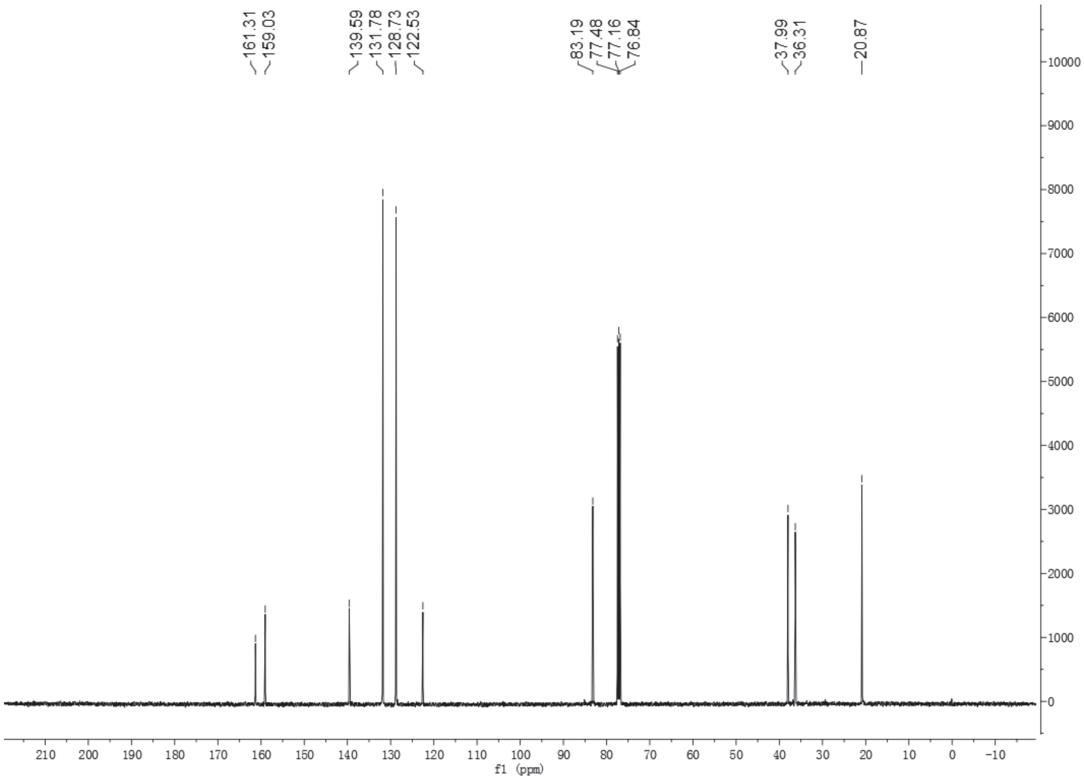

9.54
7.38
7.36
7.34
7.33
7.32
7.30
7.26
5.03
5.01
4.99
4.98
3.20
2.89
1.59
1.57
0.89
5.10
1.00
2.96
3.00
2.99
f1 (ppm)
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 -1000

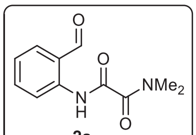

161.32
158.97
140.41
128.70
128.64
126.96
83.95
77.48
77.16
76.84
37.96
36.30
20.94
f1 (ppm)


Me
H
N
O
O
O
NMe$_2$
Br

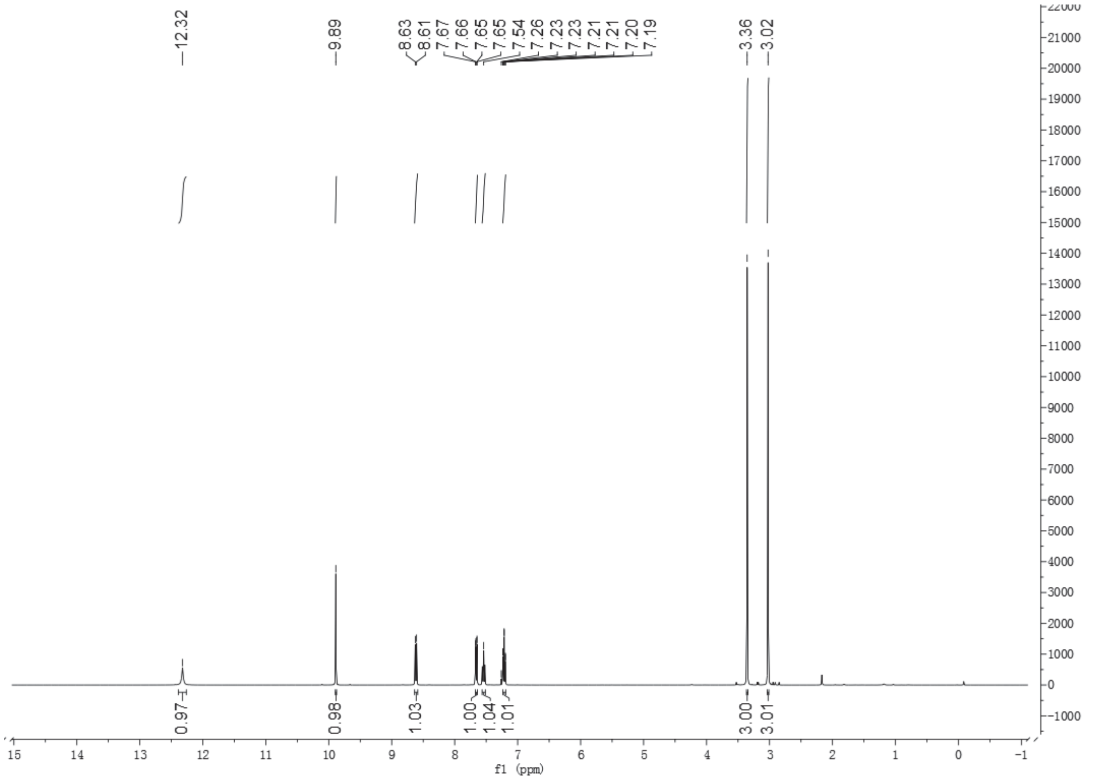
1r

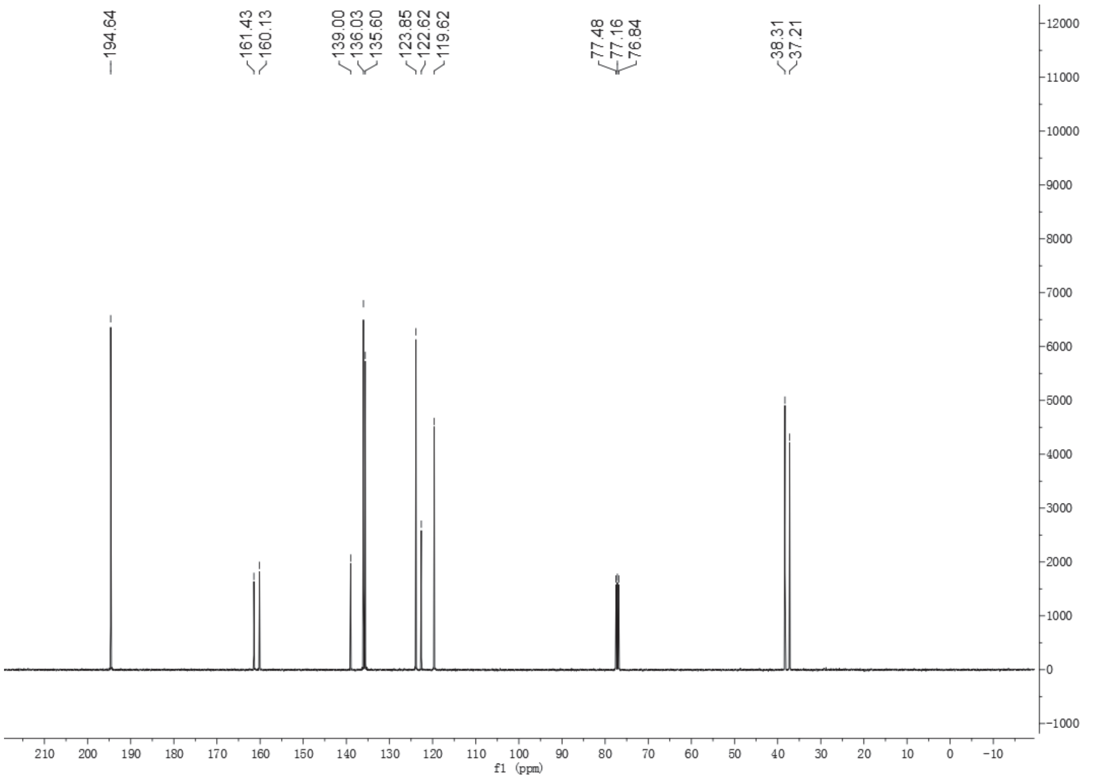

10.11
7.48
7.46
7.29
7.27
5.01
4.99
4.98
4.96
3.17
2.87
1.56
1.54
0.98
2.02
2.00
1.12
3.00
3.03
3.01
f1 (ppm)

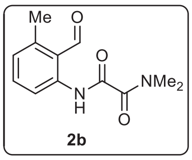

161.31
159.03
139.59
131.78
128.73
122.53
83.19
77.48
77.16
76.84
37.99
36.31
20.87
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)
10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0


O
O
N
H
NMe2
O

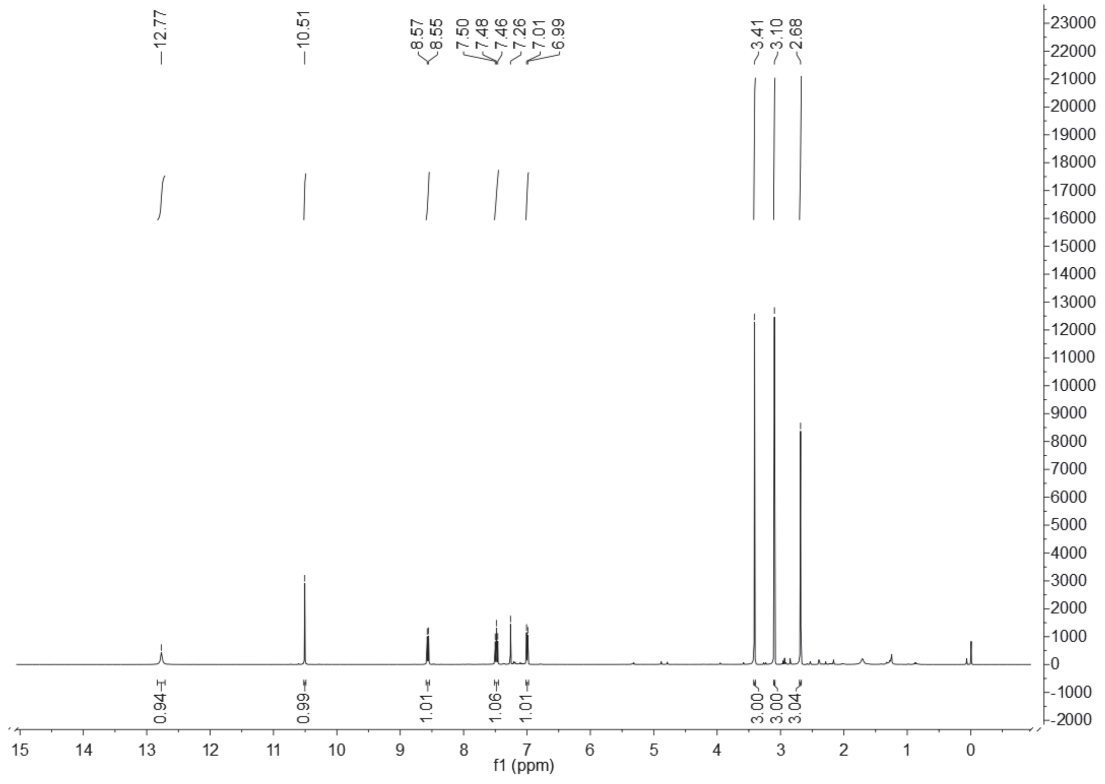
2a

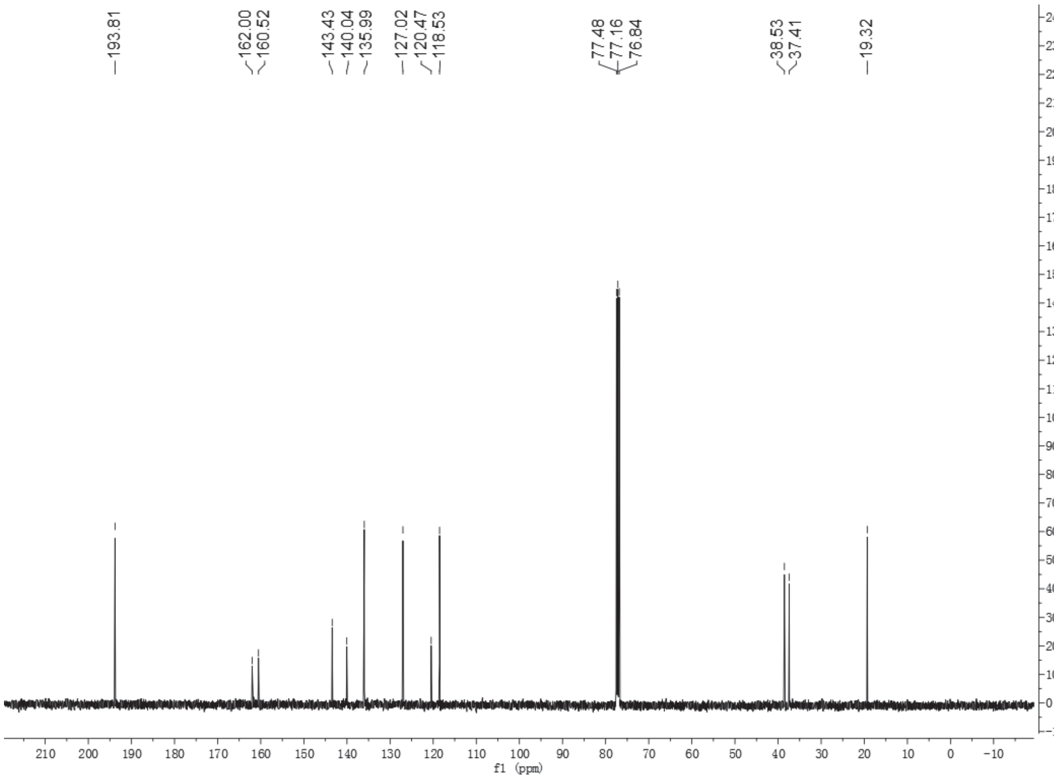

12.32
9.89
8.63
8.61
7.67
7.66
7.65
7.65
7.54
7.26
7.23
7.23
7.21
7.21
7.20
7.19
3.36
3.02
0.97
0.98
1.03
1.00
1.04
1.01
3.00
3.01
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)
22000 21000 20000 19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000

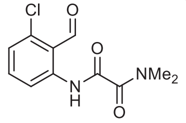

194.64
161.43
160.13
139.00
136.03
135.60
123.85
122.62
119.62
77.48
77.16
76.84
38.31
37.21
f1 (ppm)


Me
O
O
NMe2
N
H
O

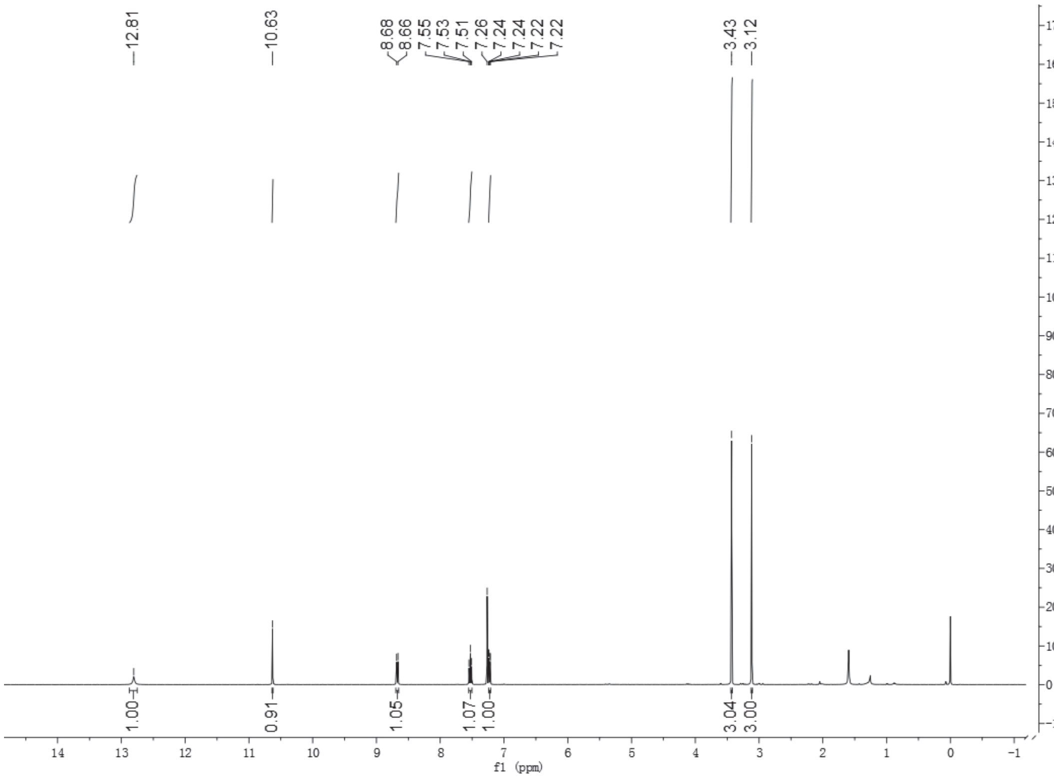
2b

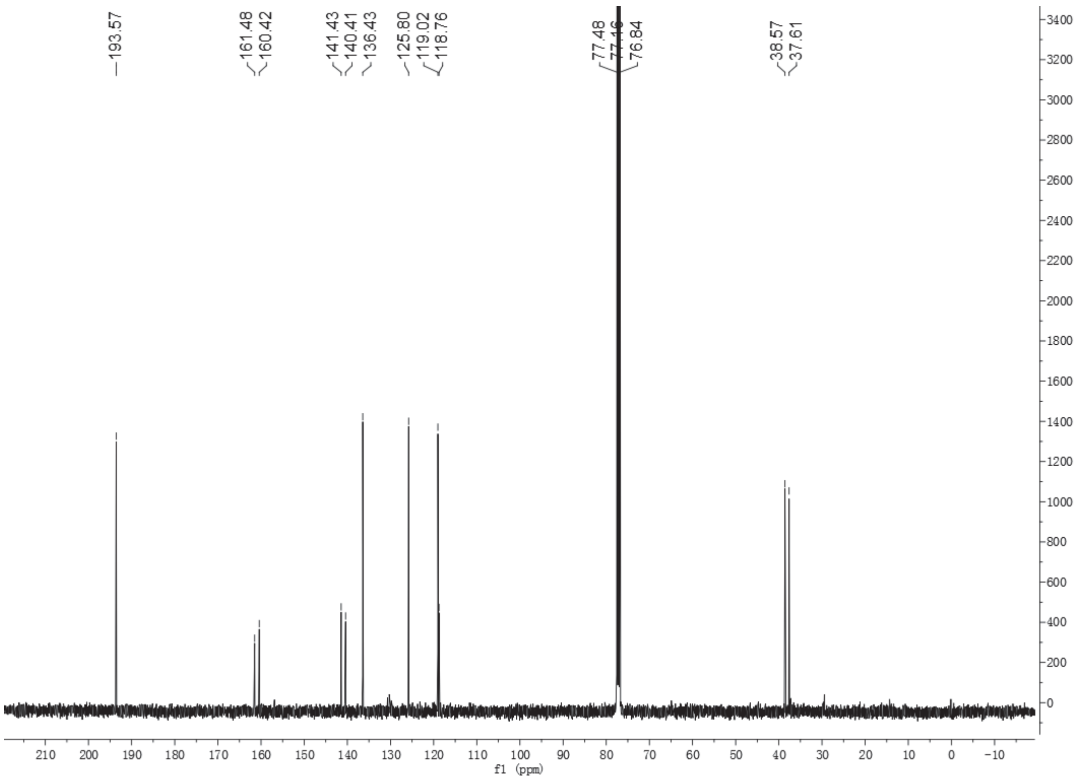

12.77
10.51
8.57
8.55
7.50
7.48
7.46
7.26
7.01
6.99
3.41
3.10
2.68
0.94
0.99
1.01
1.06
1.01
3.00
3.00
3.04
f1 (ppm)

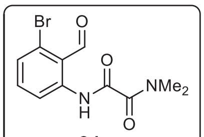

193.81
162.00
160.52
143.43
140.04
135.99
127.02
120.47
118.53
77.48
77.16
76.84
38.53
37.41
19.32
2400
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
−100
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


Cl
O
O
NMe2
N
H
O

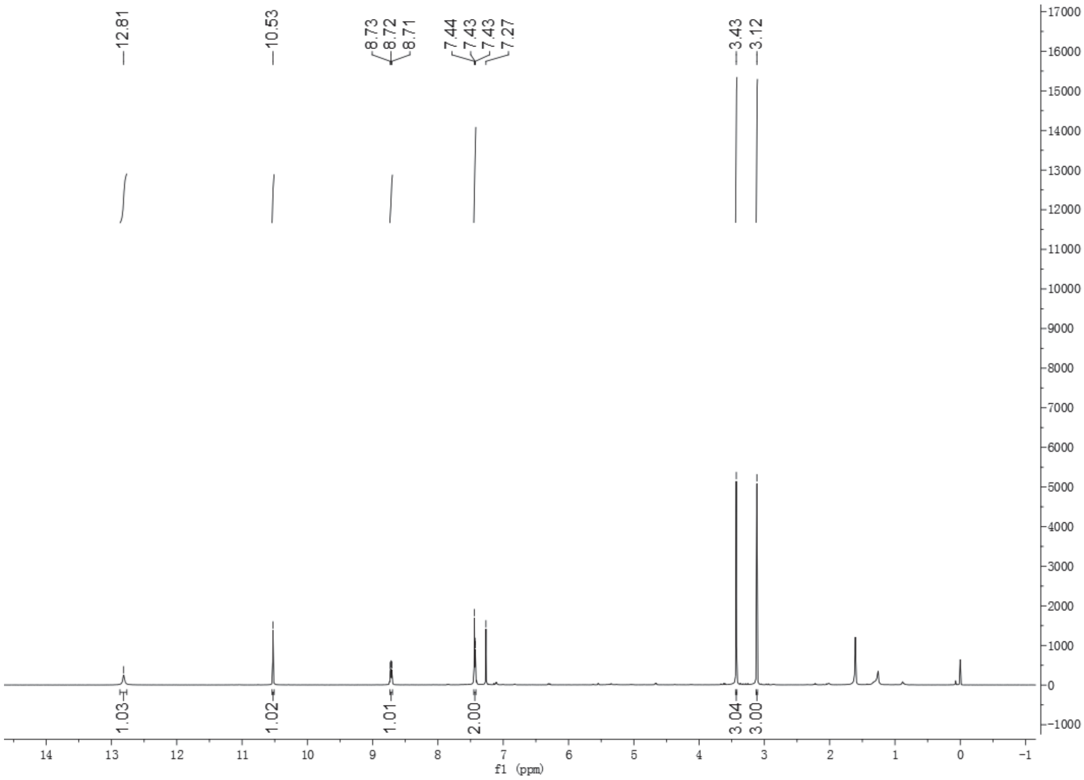
2c

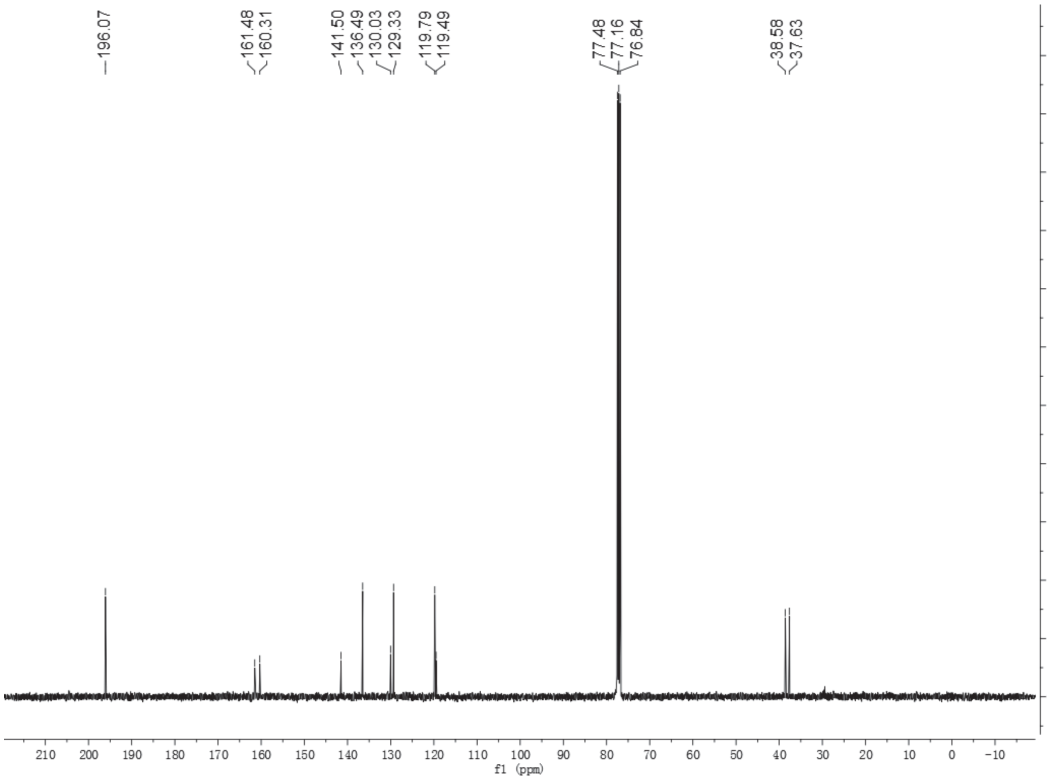

12.81
10.63
8.68
8.66
7.55
7.53
7.51
7.26
7.24
7.22
7.22
3.43
3.12
1.00
0.91
1.05
1.07
1.00
3.04
3.00
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)

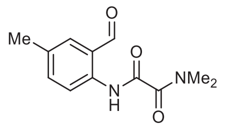

193.57
161.48
160.42
141.43
140.41
136.43
125.80
119.02
118.76
77.48
77.16
76.84
38.57
37.61
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0


Br
O
O
NMe$_2$
N
H
O

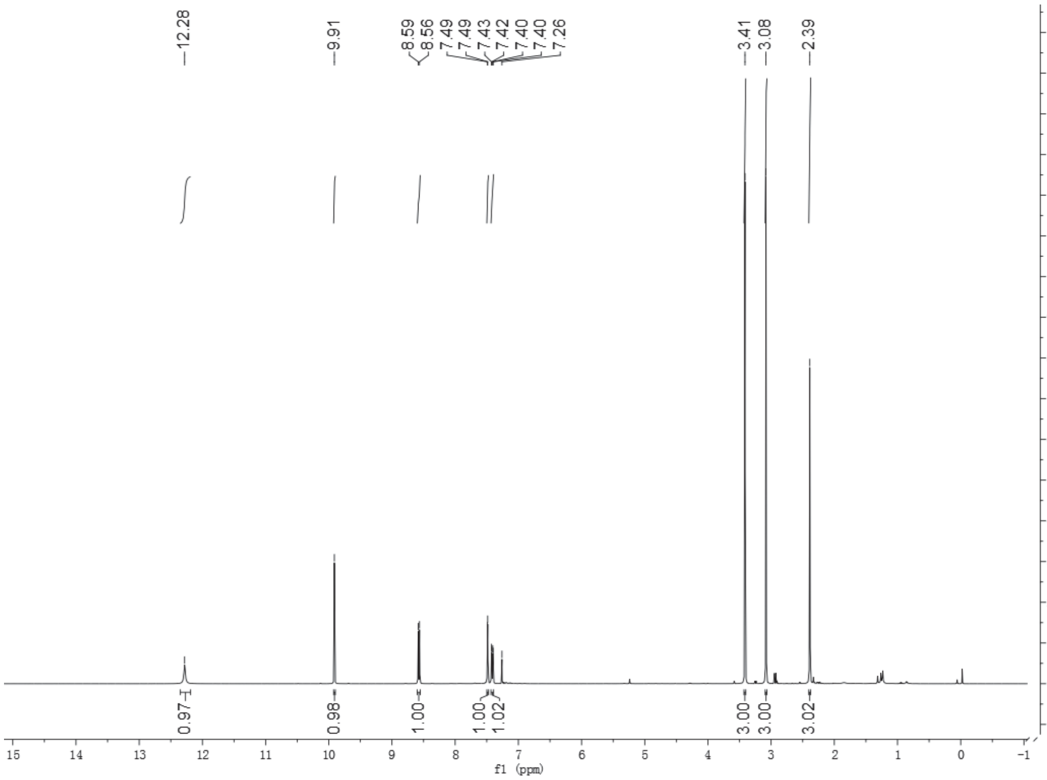
2d

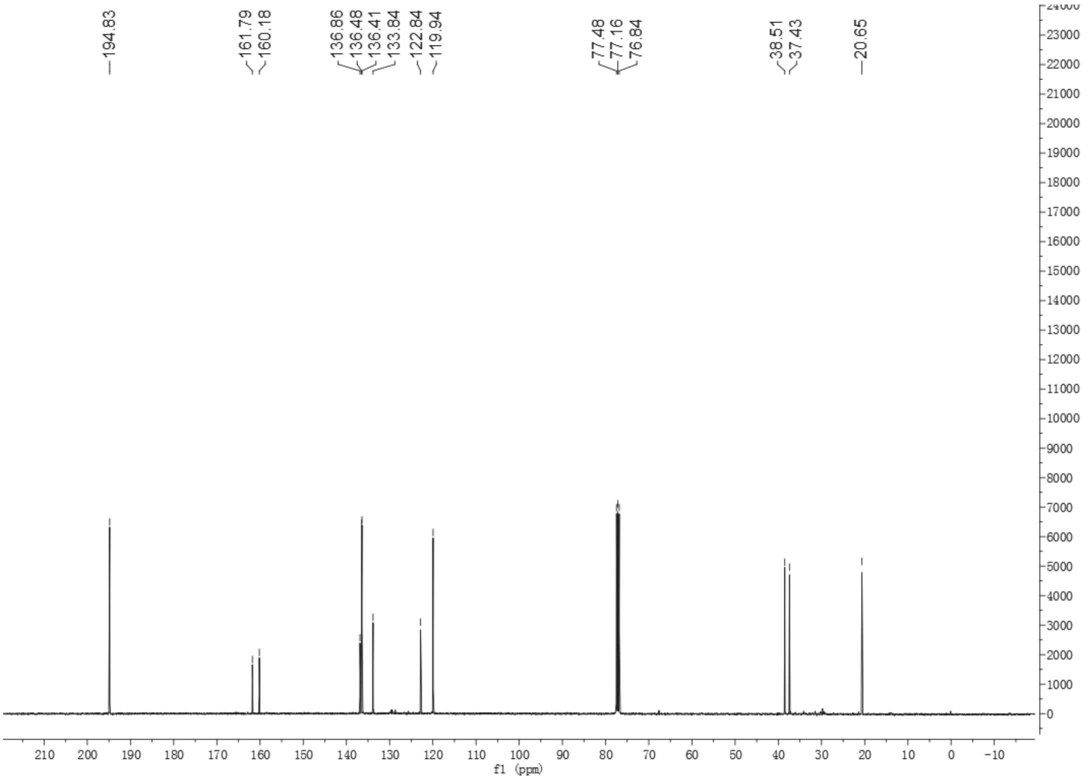

12.81
10.53
8.73
8.72
8.71
7.44
7.43
7.43
7.27
3.43
3.12
1.03
1.02
1.01
2.00
3.04
3.00
f1 (ppm)
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 -1000

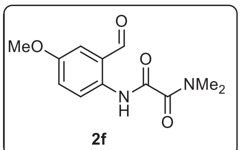

196.07
161.48
160.31
141.50
136.49
130.03
129.33
119.79
119.49
77.48
77.16
76.84
38.58
37.63
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


Me
O
O
NMe2
N
H
O

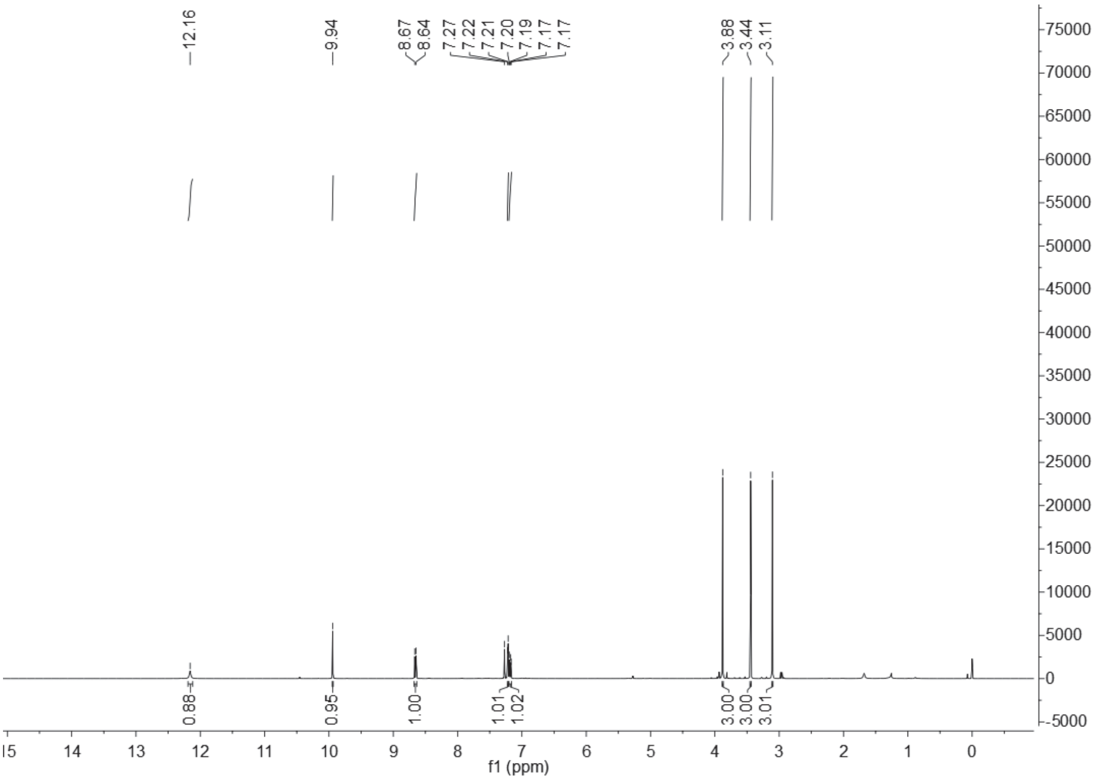
2e

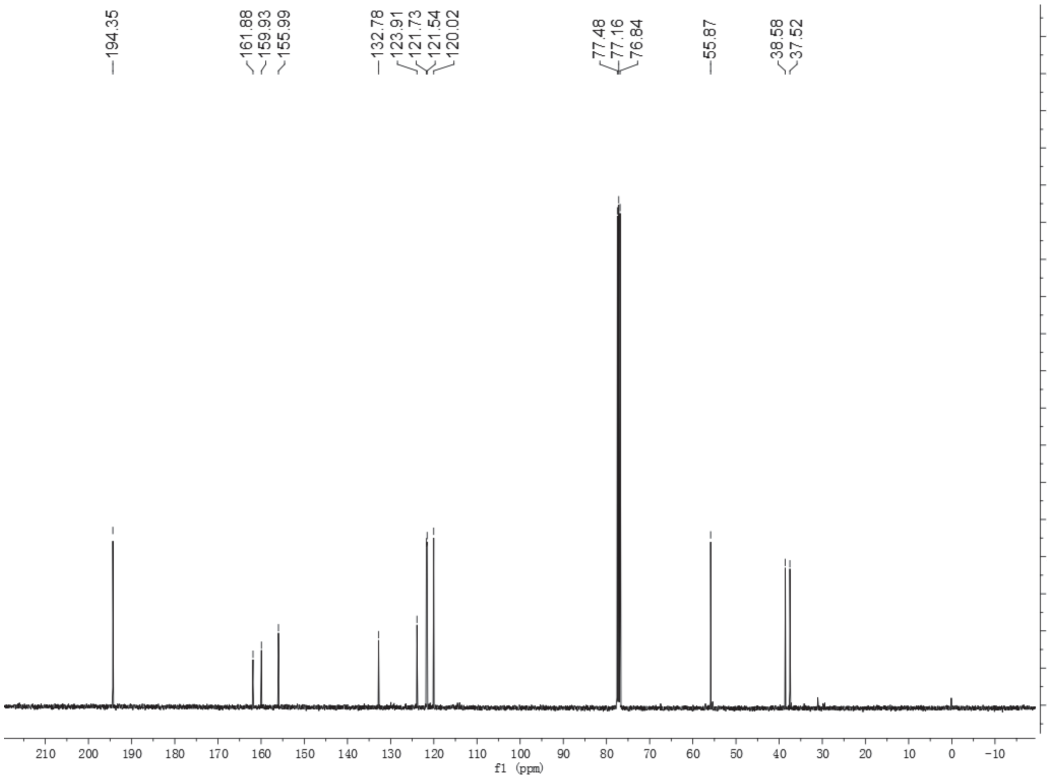

12.28
9.91
8.59
8.56
7.49
7.49
7.43
7.42
7.40
7.40
7.26
3.41
3.08
2.39
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
0.97
0.98
1.00
1.00
1.02
3.00
3.00
3.02
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)

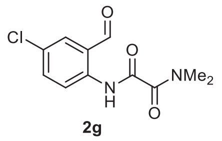

194.83
161.79
160.18
136.86
136.48
136.41
133.84
122.84
119.94
77.48
77.16
76.84
38.51
37.43
20.65
f1 (ppm)


MeO
O
O
NMe2
N
H
O

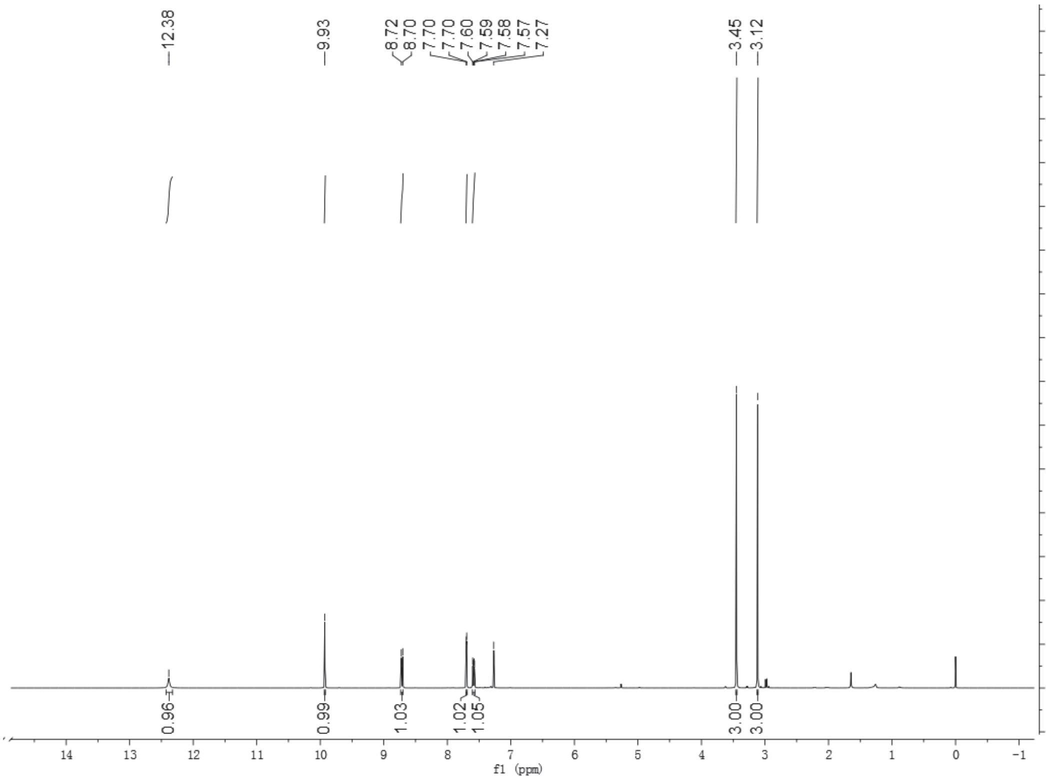
2f

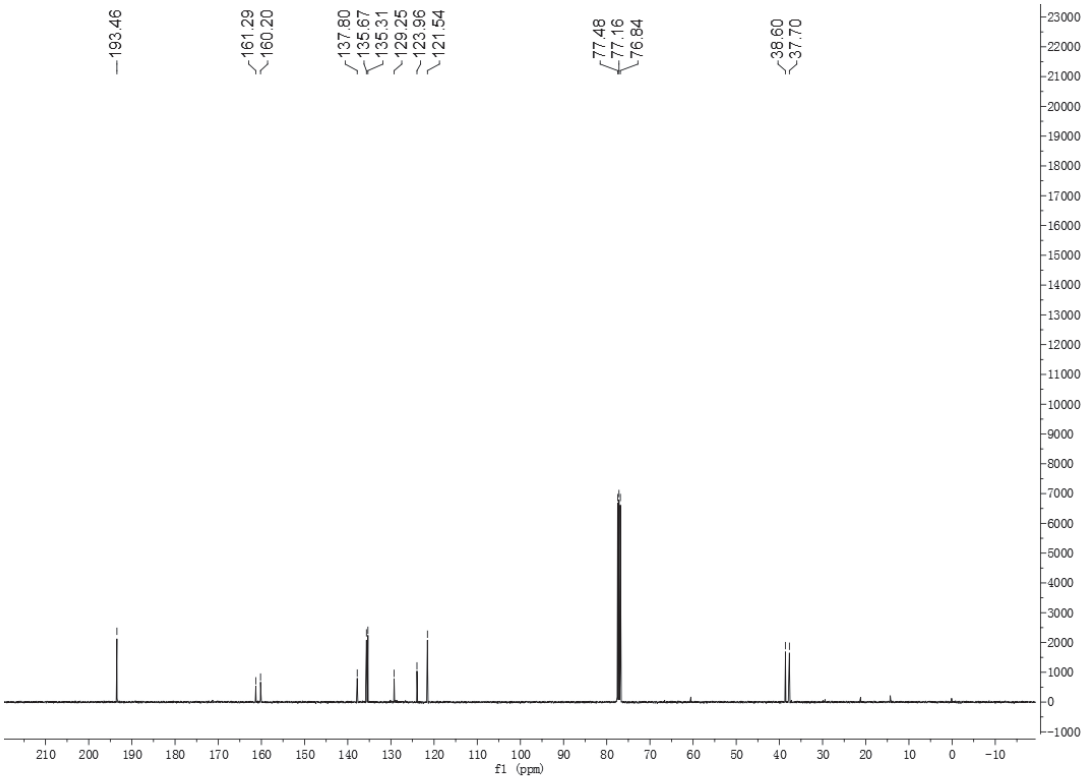

12.16
9.94
8.67
8.64
7.27
7.22
7.21
7.20
7.19
7.17
7.17
3.88
3.44
3.11
0.88
0.95
1.00
1.01
1.02
3.00
3.00
3.01
f1 (ppm)

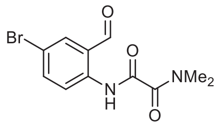

194.35
161.88
159.93
155.99
132.78
123.91
121.73
121.54
120.02
77.48
77.16
76.84
55.87
38.58
37.52
f1 (ppm)


Cl
O
O
NMe$_2$
N
H
O

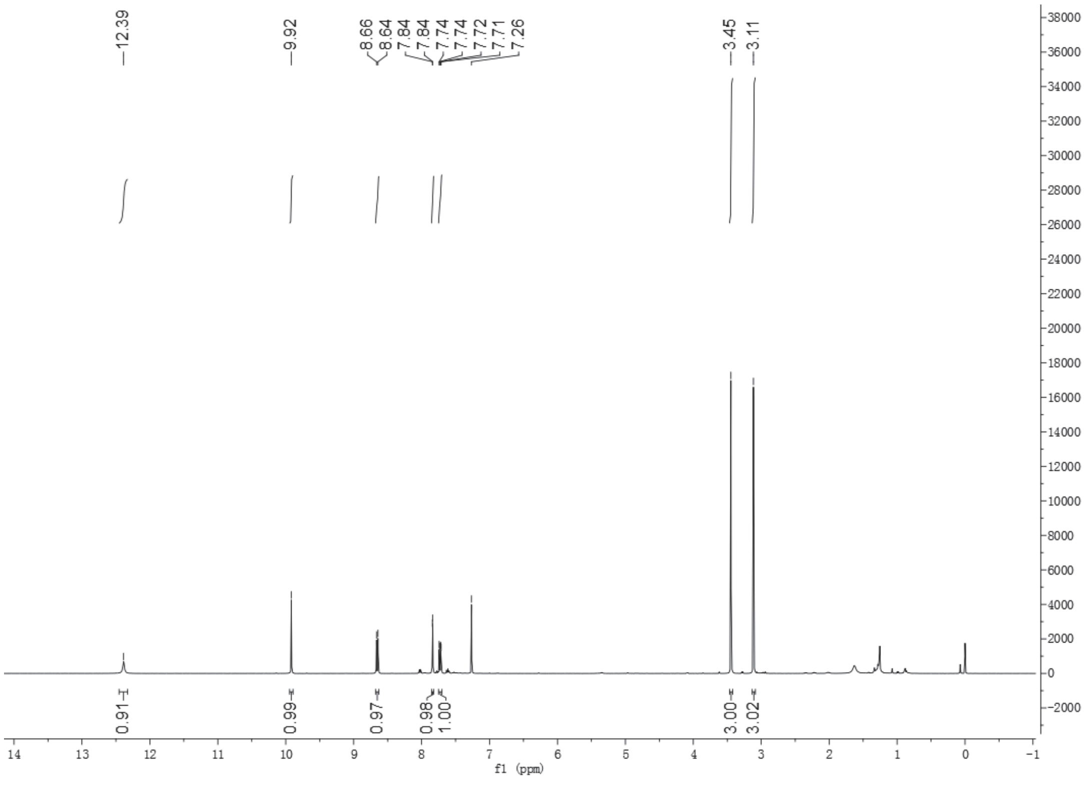
2g

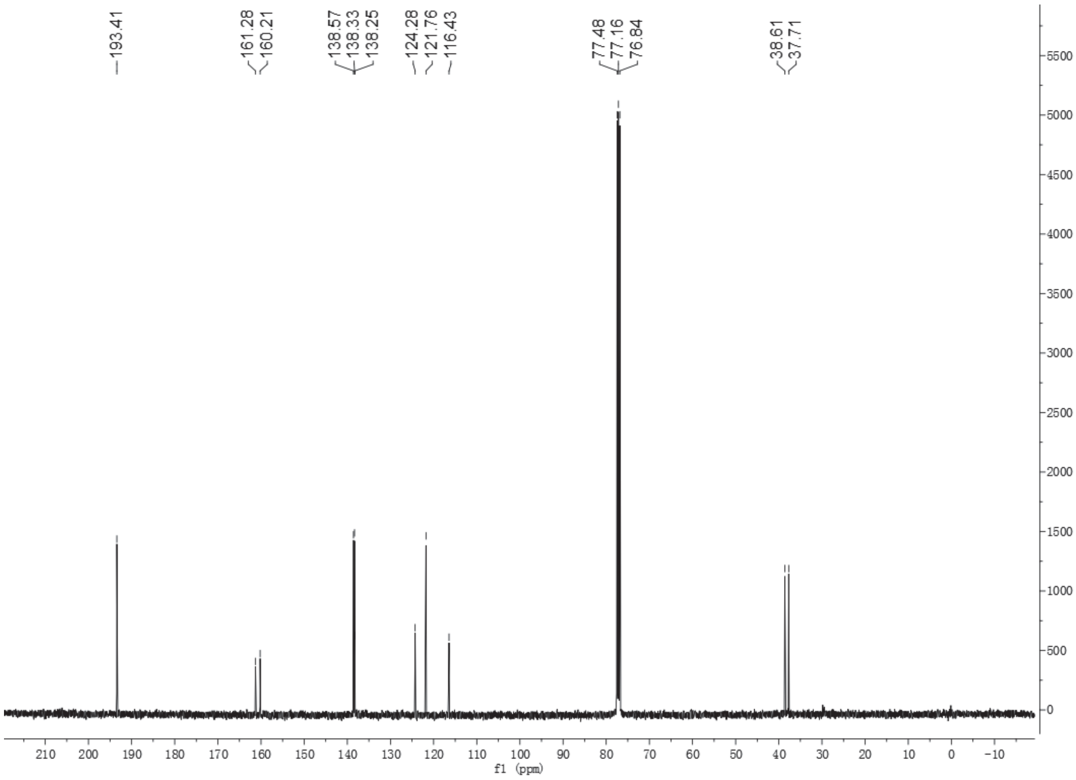

12.38
9.93
8.72
8.70
7.70
7.70
7.60
7.59
7.58
7.57
7.27
3.45
3.12
0.96
0.99
1.03
1.02
1.05
3.00
3.00
f1 (ppm)

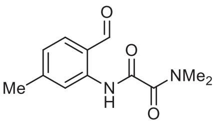

193.46
161.29
160.20
137.80
135.67
135.31
129.25
123.96
121.54
77.48
77.16
76.84
38.60
37.70
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


Br
O
O
N
H
NMe2
O

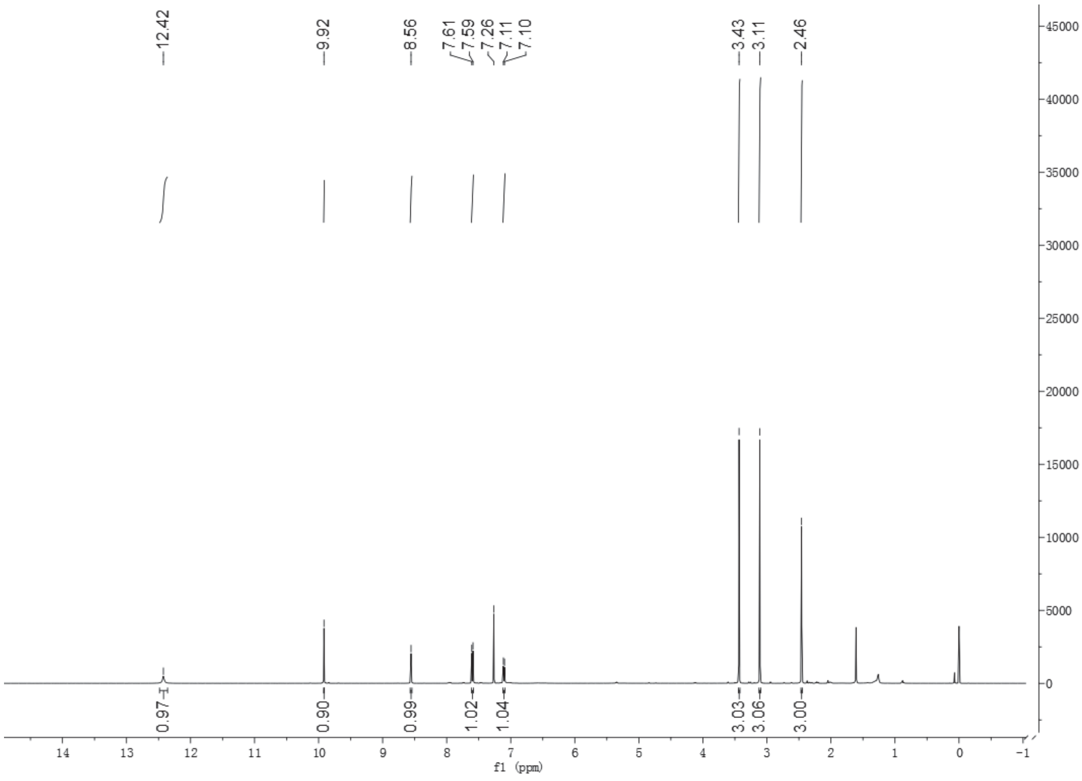
2h

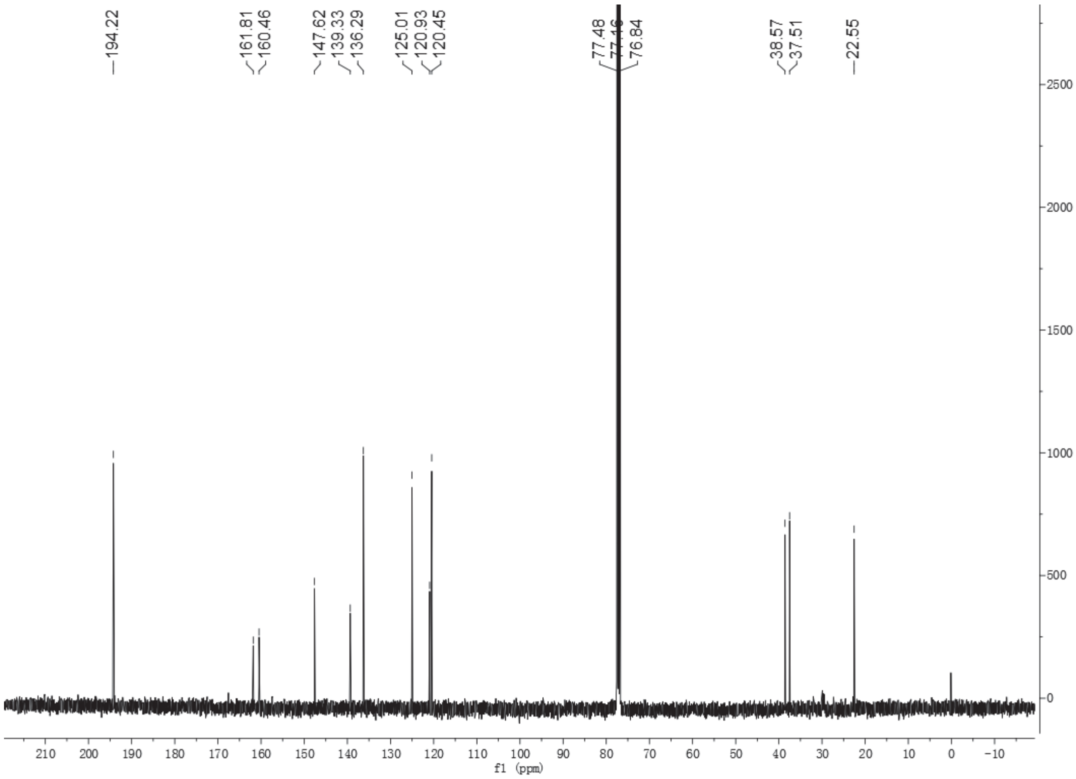

12.39
9.92
8.66
8.64
7.84
7.84
7.74
7.74
7.72
7.71
7.26
3.45
3.11
0.91
0.99
0.97
0.98
1.00
3.00
3.02
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
−2000
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)

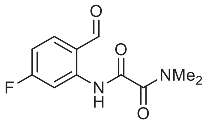

193.41
161.28
160.21
138.57
138.33
138.25
124.28
121.76
116.43
77.48
77.16
76.84
38.61
37.71
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


O
O
Me
N
H
NMe2
O

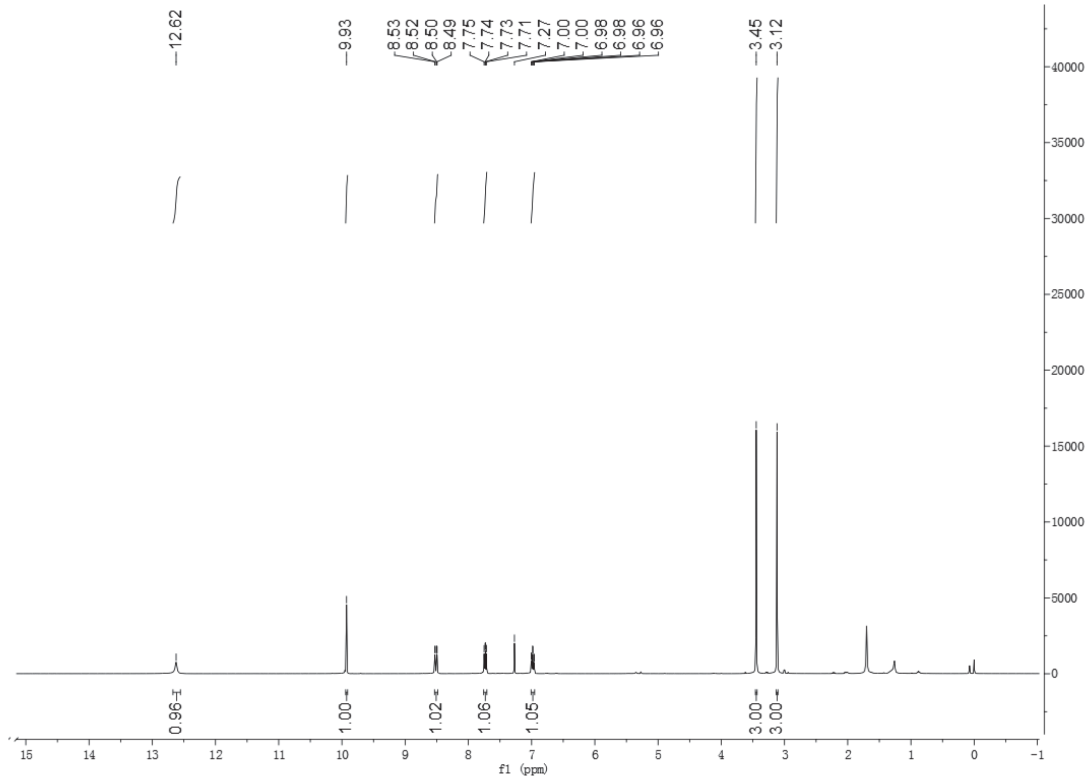
2i

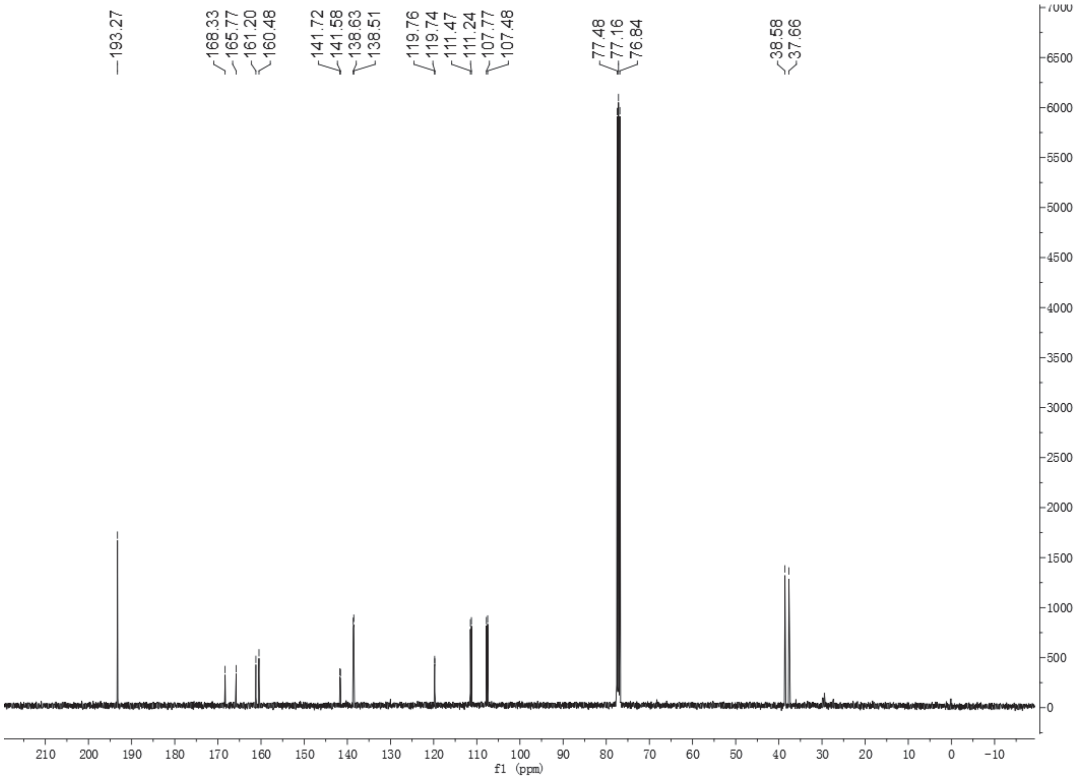

12.42
9.92
8.56
7.61
7.59
7.26
7.11
7.10
3.43
3.11
2.46
0.97
0.90
0.99
1.02
1.04
3.03
3.06
3.00
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)

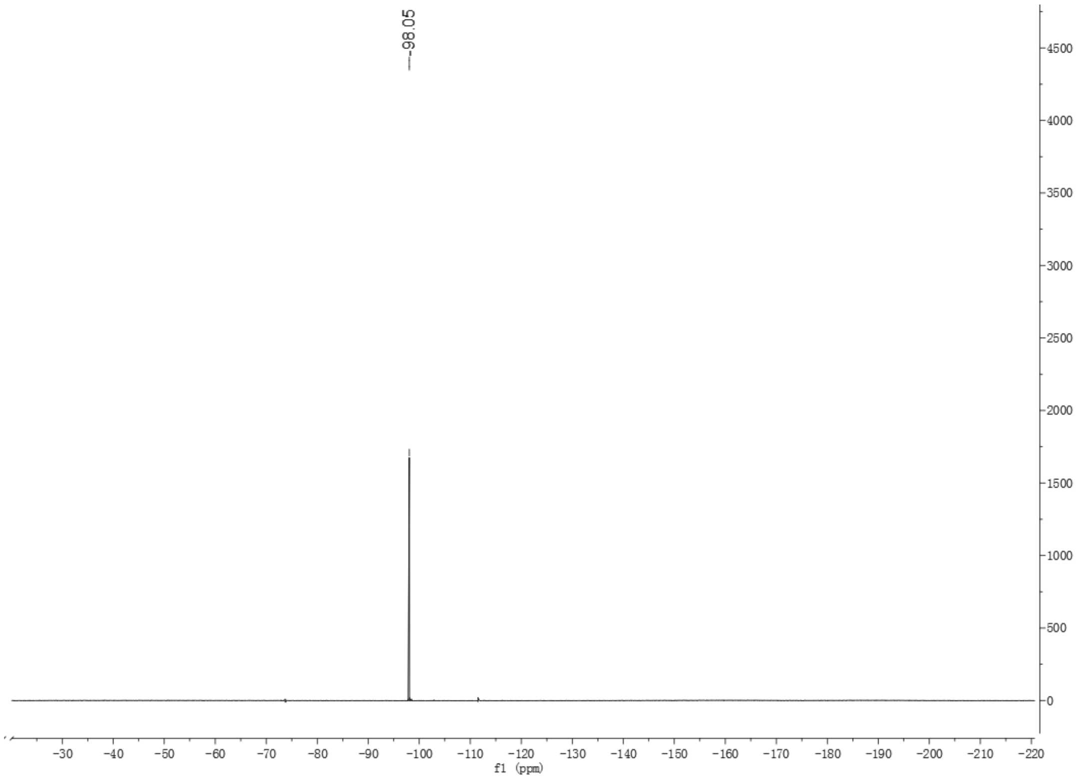

194.22
161.81
160.46
147.62
139.33
136.29
125.01
120.93
120.45
77.48
77.16
76.84
38.57
37.51
22.55
2500
2000
1500
1000
500
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

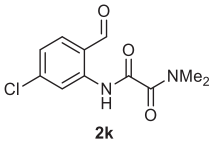

O
F
N
H
O
O
NMe2

2j

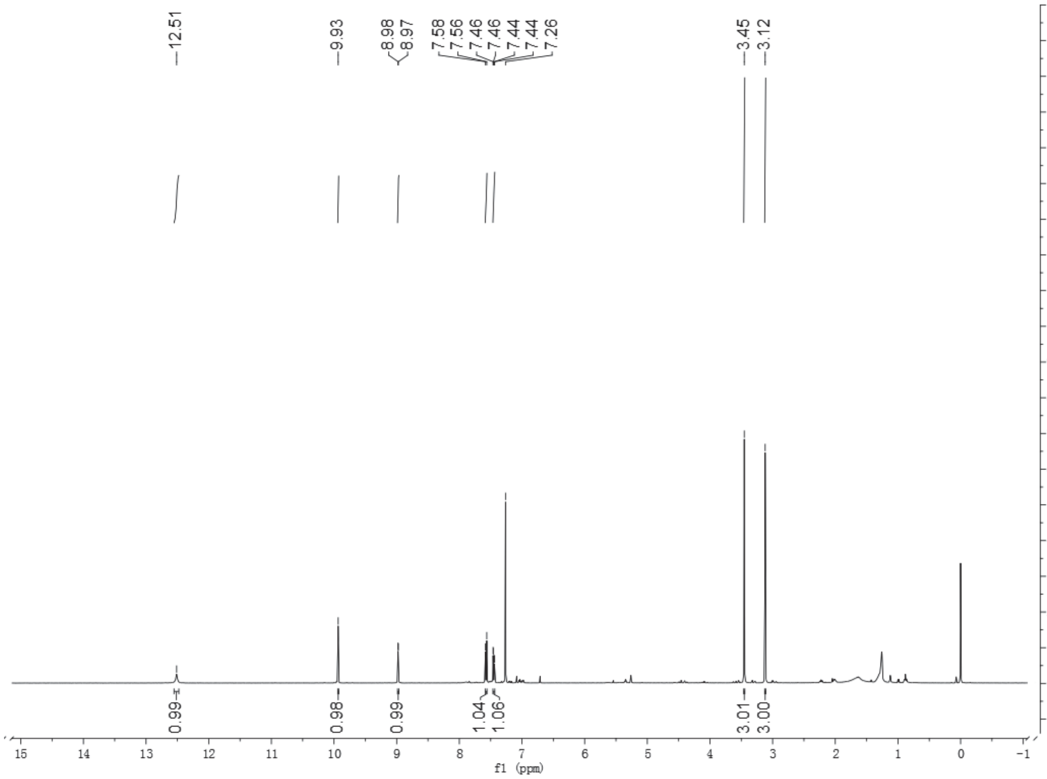

12.62
9.93
8.53
8.52
8.50
8.49
7.75
7.74
7.73
7.71
7.27
7.00
7.00
6.98
6.98
6.96
6.96
3.45
3.12
40000
35000
30000
25000
20000
15000
10000
5000
0
0.96
1.00
1.02
1.06
1.05
3.00
3.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)

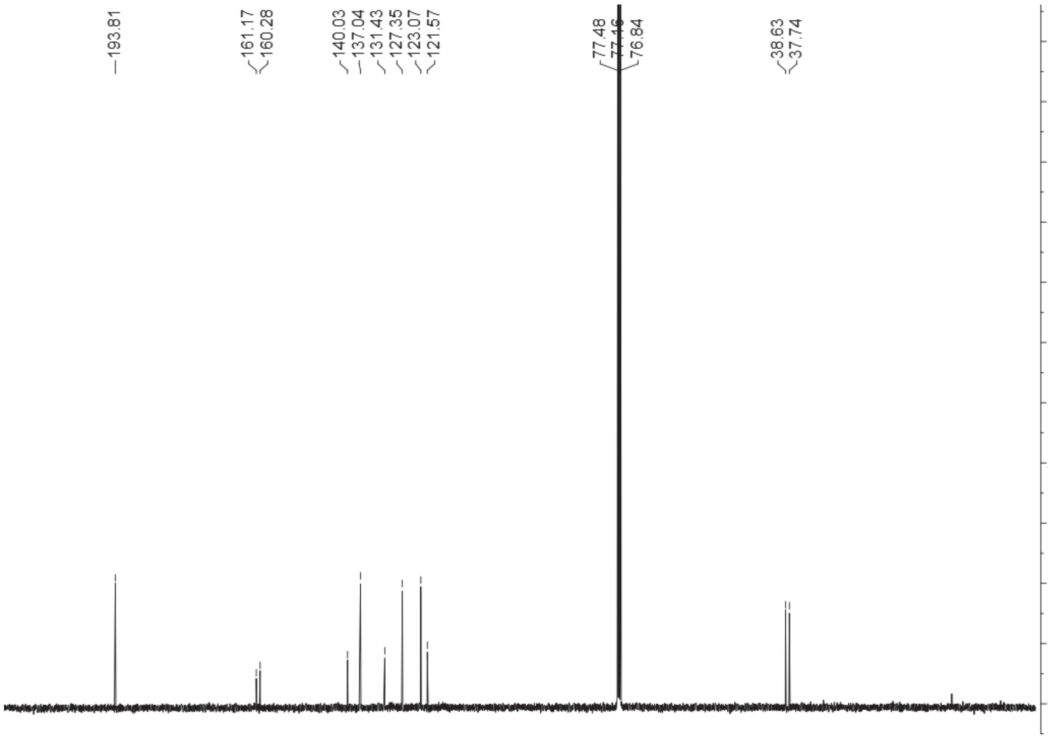

193.27
168.33
165.77
161.20
160.48
141.72
141.58
138.63
138.51
119.76
119.74
111.47
111.24
107.77
107.48
77.48
77.16
76.84
38.58
37.66
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

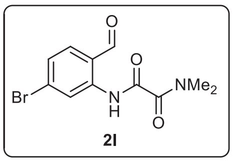

−98.05
4500
4000
3500
3000
2500
2000
1500
1000
500
0
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
−220
f1 (ppm)


O
O
Cl
N
H
NMe2
O

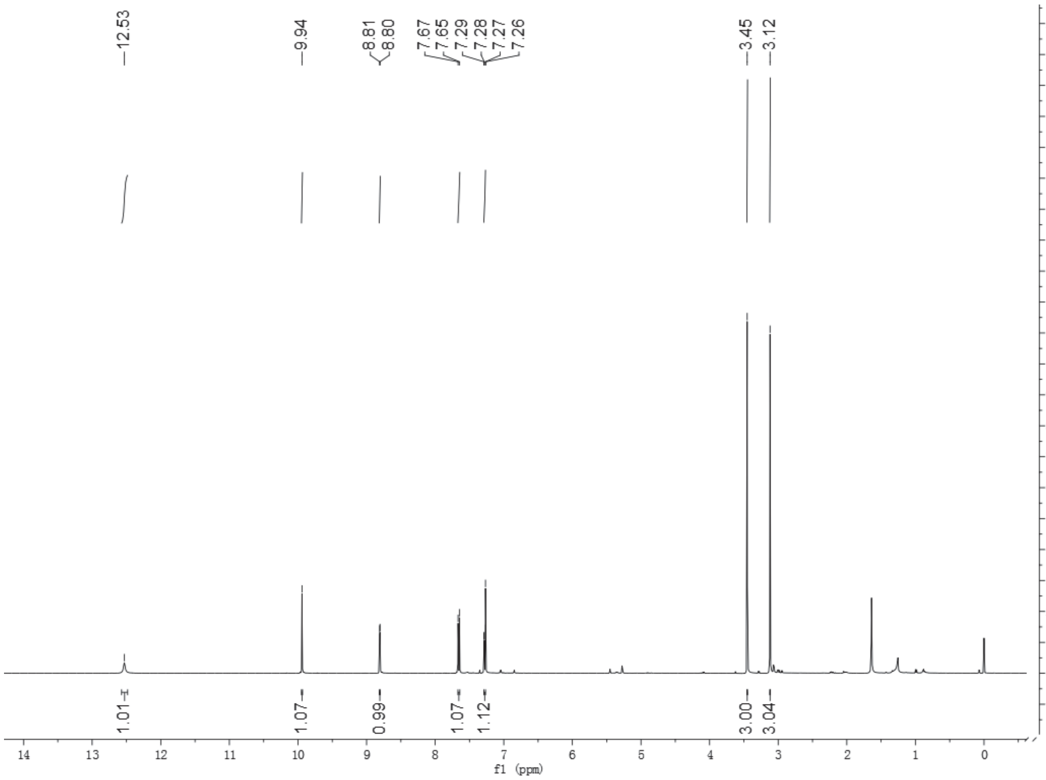
2k

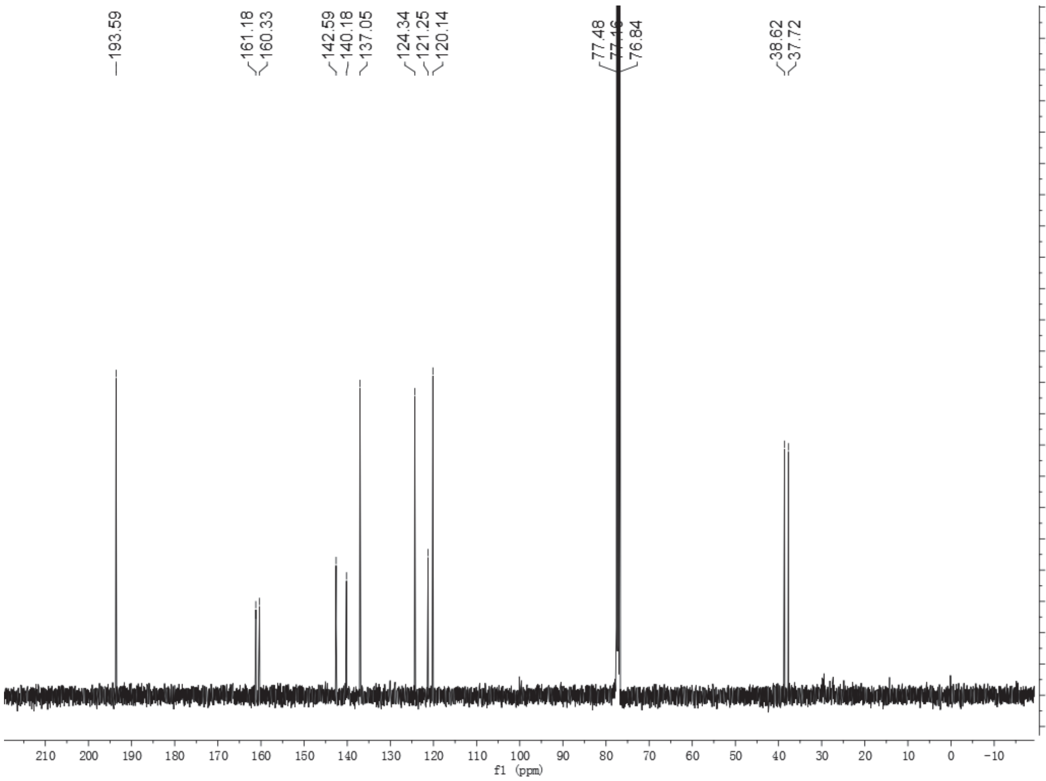

12.51
9.93
8.98
8.97
7.58
7.56
7.46
7.46
7.44
7.44
7.26
3.45
3.12
0.99
0.98
0.99
1.04
1.06
3.01
3.00
f1 (ppm)
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000

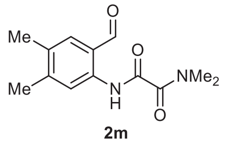

193.81
161.17
160.28
140.03
137.04
131.43
127.35
123.07
121.57
77.48
77.16
76.84
38.63
37.74
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0


Br
O
O
NMe2
N
H
O

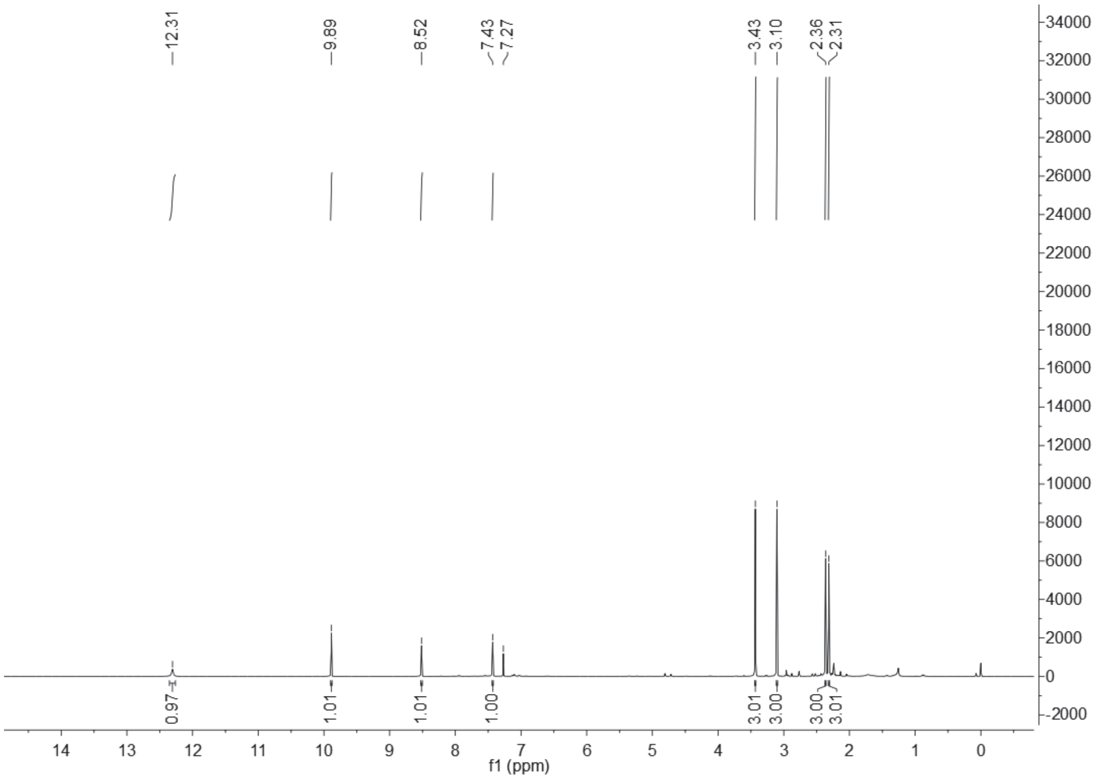
2l

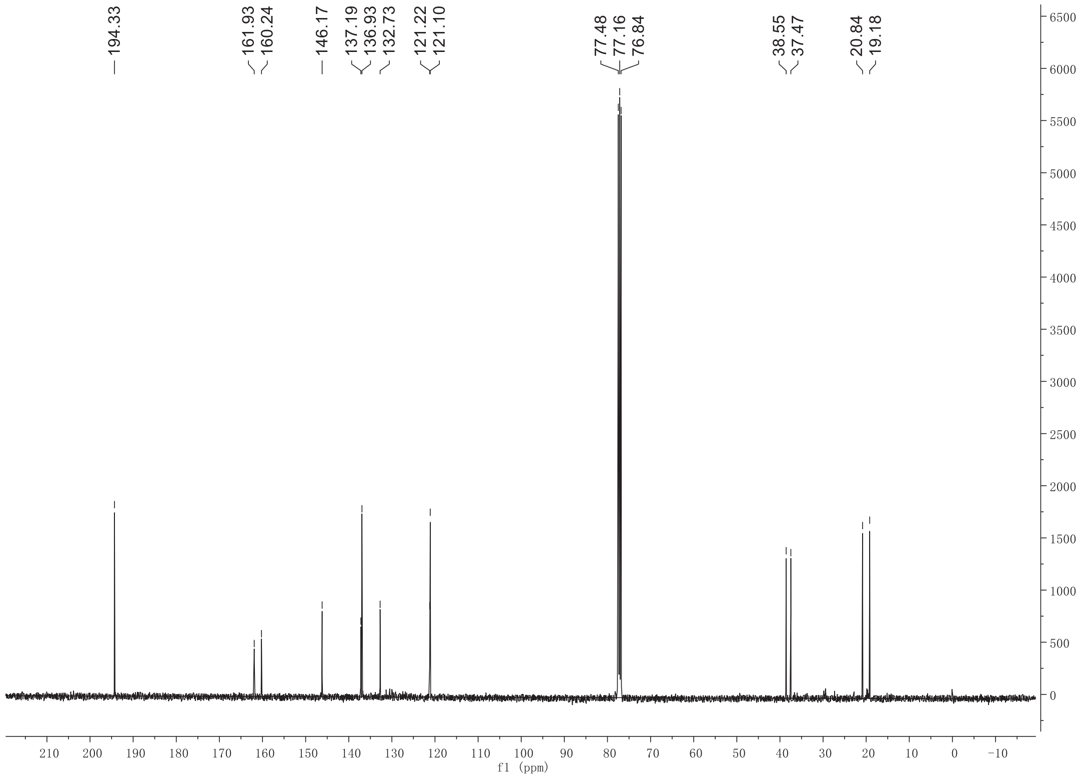

12.53
9.94
8.81
8.80
7.67
7.65
7.29
7.28
7.27
7.26
3.45
3.12
1.01
1.07
0.99
1.07
1.12
3.00
3.04
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

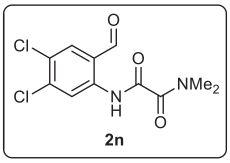

193.59
161.18
160.33
142.59
140.18
137.05
124.34
121.25
120.14
77.48
77.16
76.84
38.62
37.72
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100


Me
Me
O
O
O
N
H
NMe2

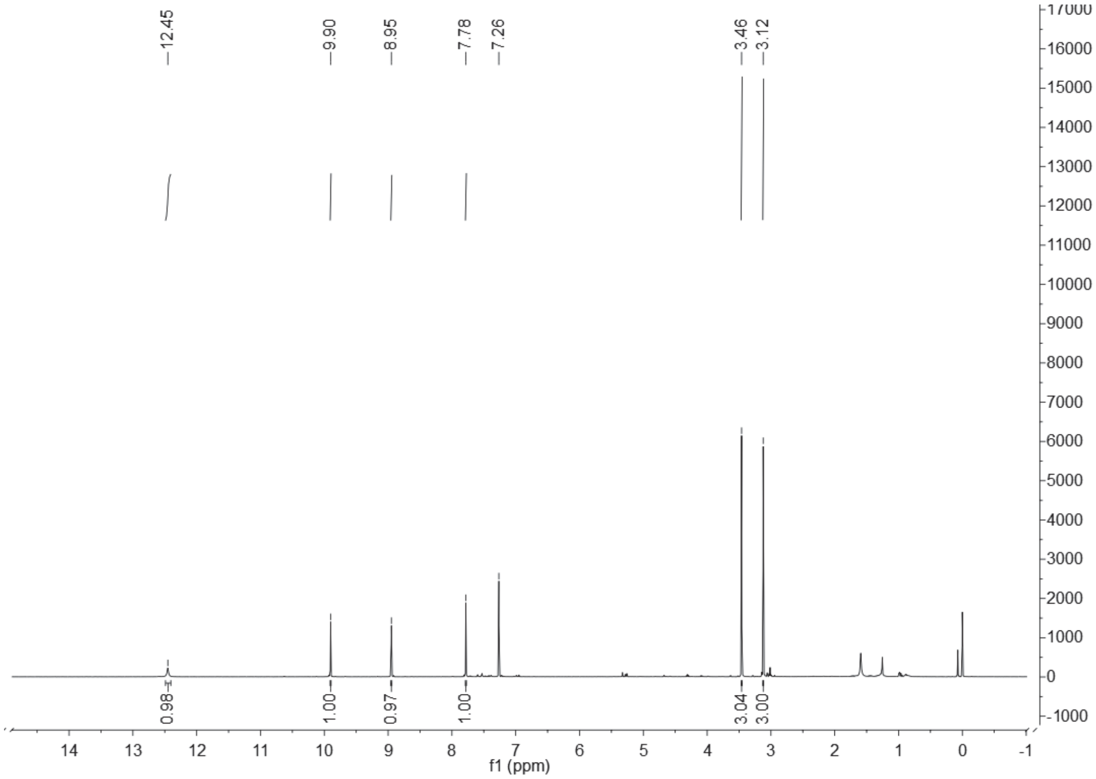
2m

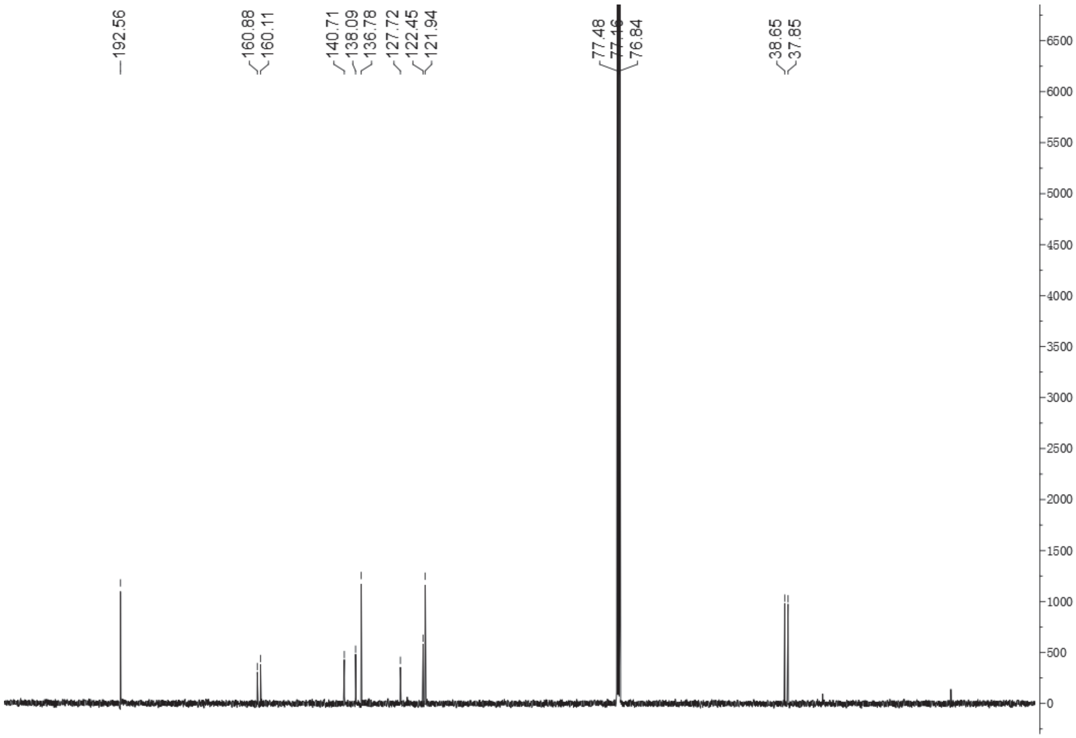

12.31
9.89
8.52
7.43
7.27
3.43
3.10
2.36
2.31
0.97
1.01
1.01
1.00
3.01
3.00
3.00
3.01
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)
34000 32000 30000 28000 26000 24000 22000 20000 18000 16000 14000 12000 10000 8000 6000 4000 2000 0 -2000

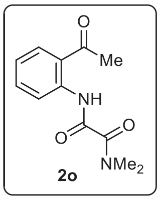

194.33
161.93
160.24
146.17
137.19
136.93
132.73
121.22
121.10
77.48
77.16
76.84
38.55
37.47
20.84
19.18
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
6500 6000 5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0


O
Cl
Cl
O
NMe$_2$
N
H
O

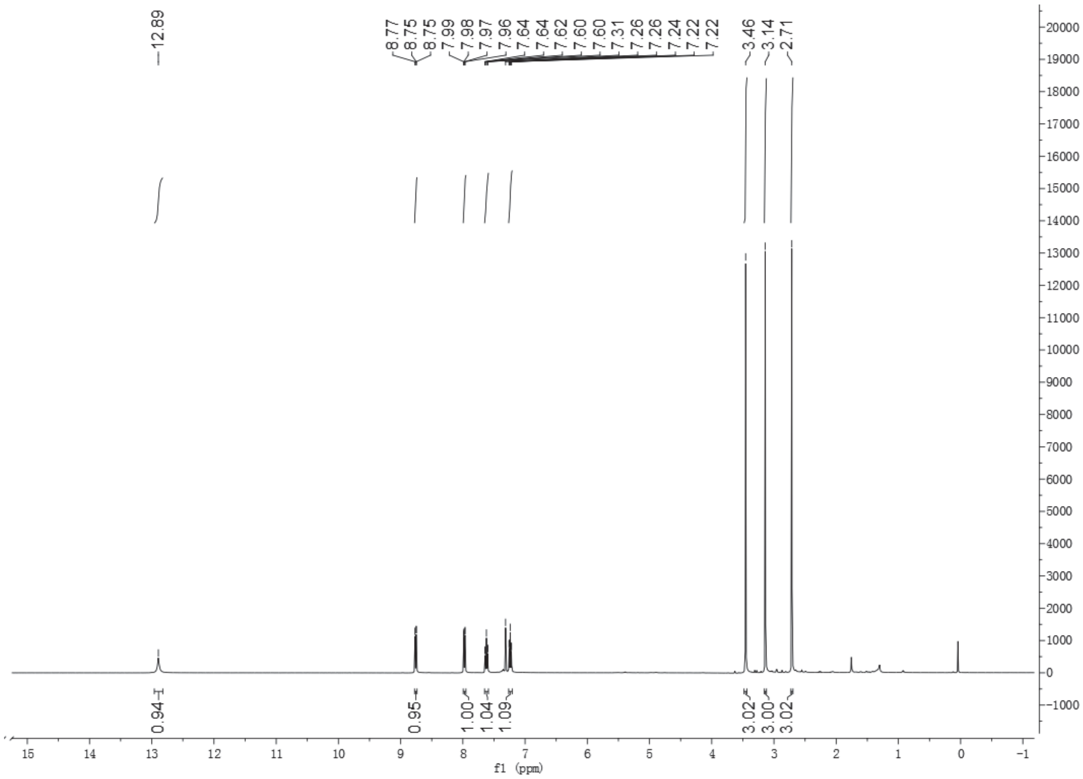
2n

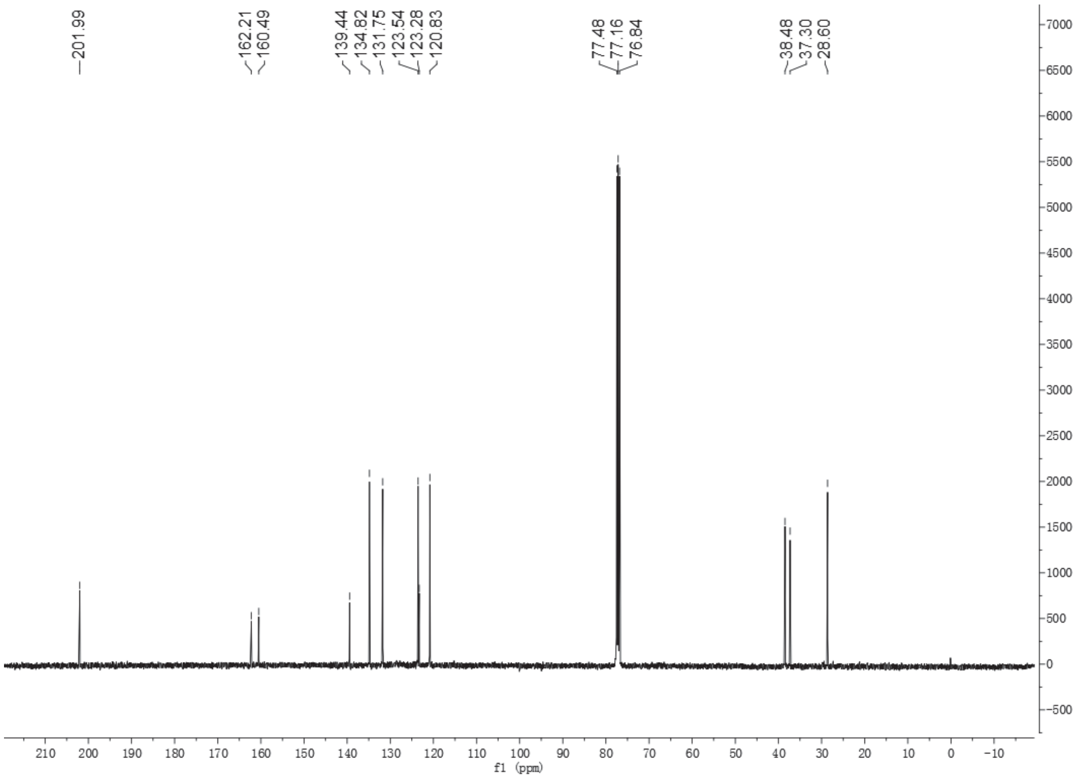

12.45
9.90
8.95
7.78
7.26
3.46
3.12
0.98
1.00
0.97
1.00
3.04
3.00
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

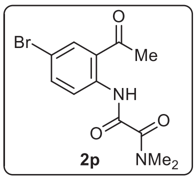

192.56
160.88
160.11
140.71
138.09
136.78
127.72
122.45
121.94
77.48
77.16
76.84
38.65
37.85
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
Me
NH
O
O
NMe2

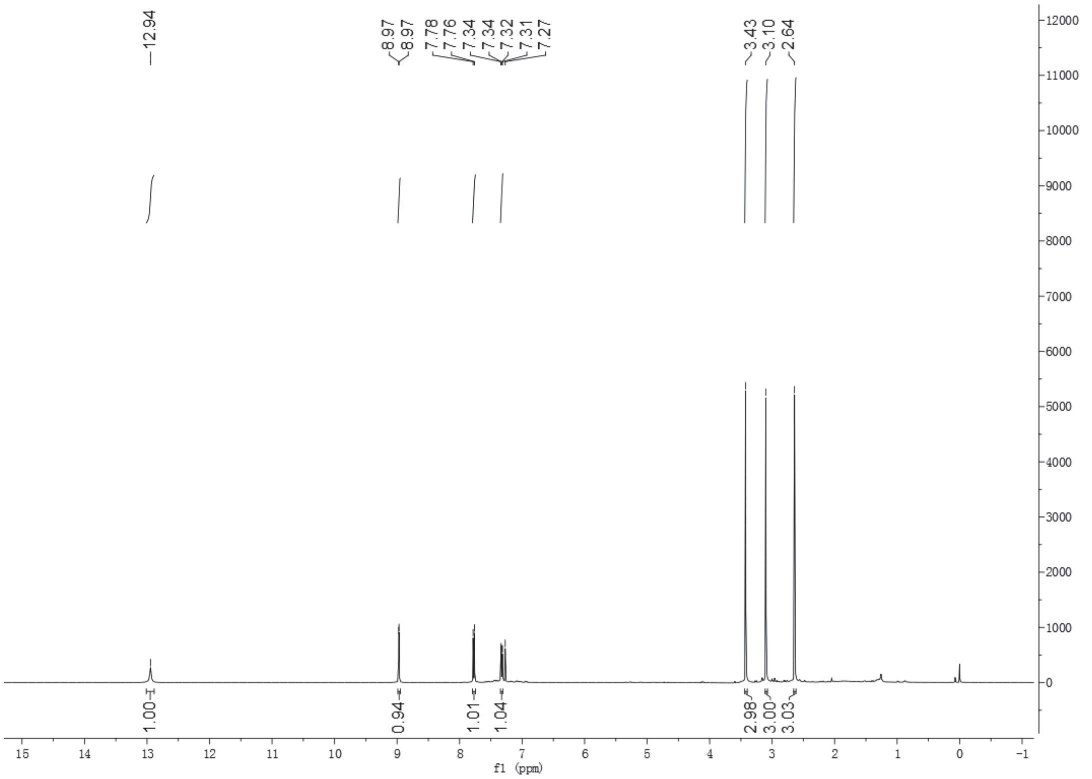
2o

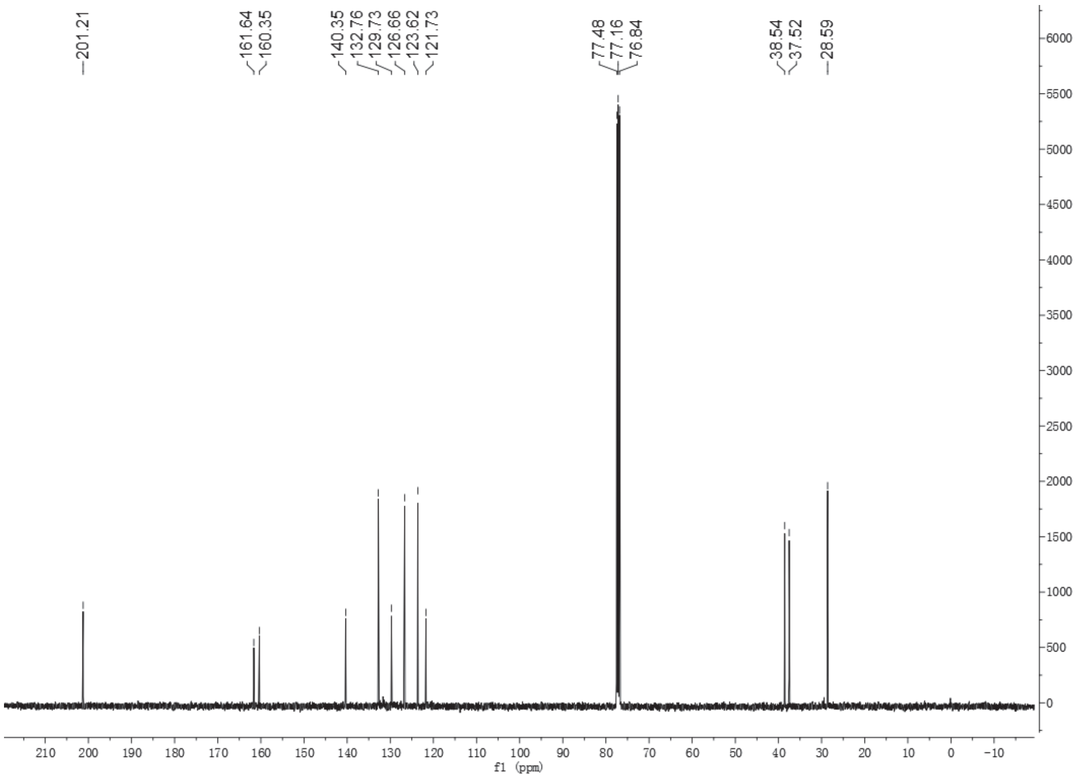

12.89
8.77
8.75
8.75
7.99
7.98
7.97
7.96
7.64
7.64
7.62
7.60
7.60
7.31
7.26
7.26
7.24
7.22
7.22
3.46
3.14
2.71
0.94
0.95
1.00
1.04
1.09
3.02
3.00
3.02
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

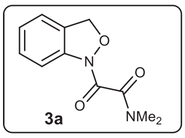

201.99
162.21
160.49
139.44
134.82
131.75
123.54
123.28
120.83
77.48
77.16
76.84
38.48
37.30
28.60
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500


Br
O
Me
NH
O
O
NMe2

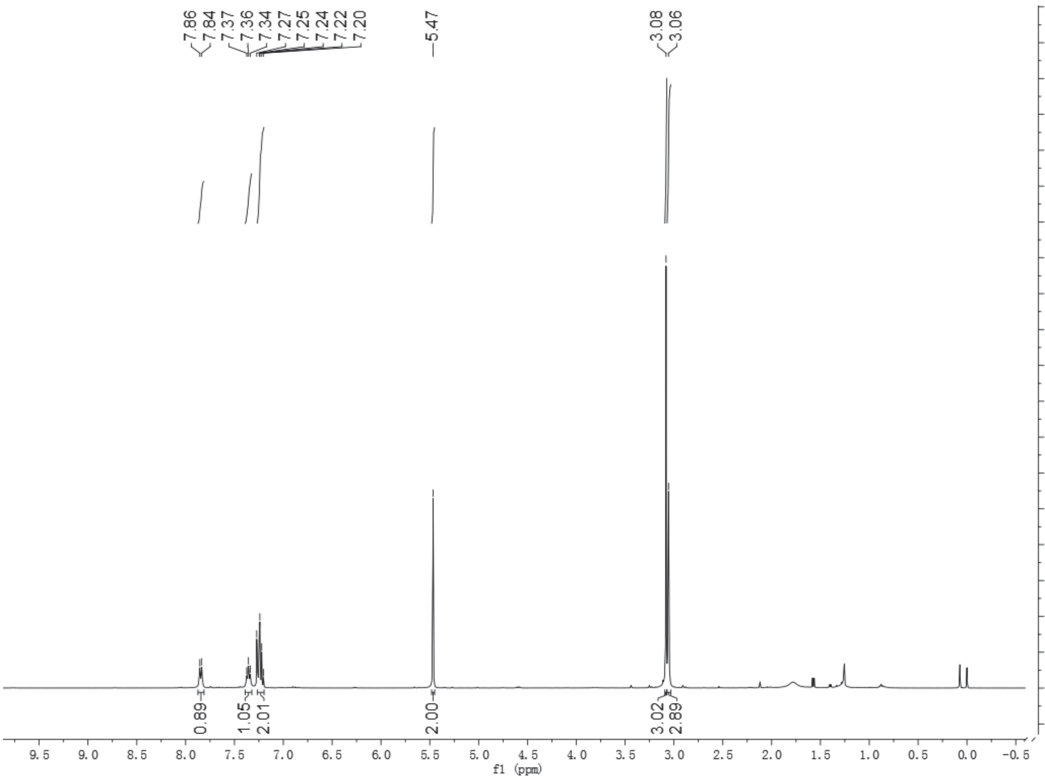
2p

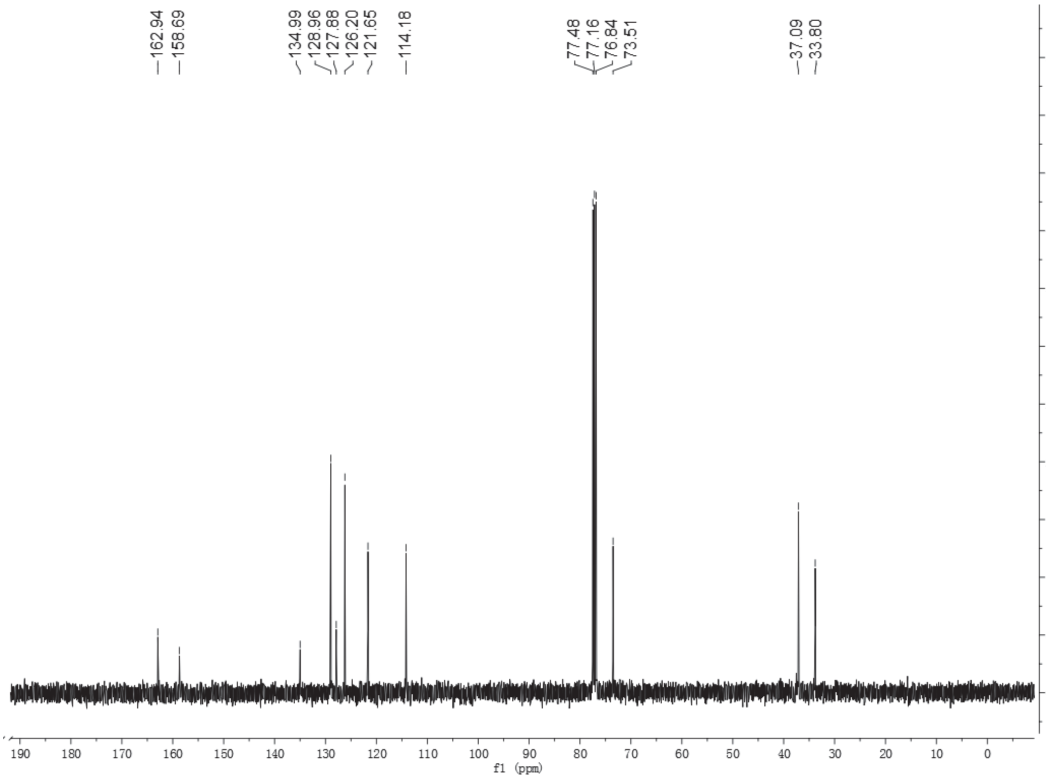

12.94
8.97
8.97
7.78
7.76
7.34
7.34
7.32
7.31
7.27
3.43
3.10
2.64
1.00
0.94
1.01
1.04
2.98
3.00
3.03
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

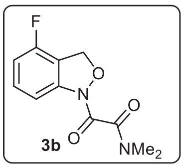

201.21
161.64
160.35
140.35
132.76
129.73
126.66
123.62
121.73
77.48
77.16
76.84
38.54
37.52
28.59
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
N
O
NMe2
O

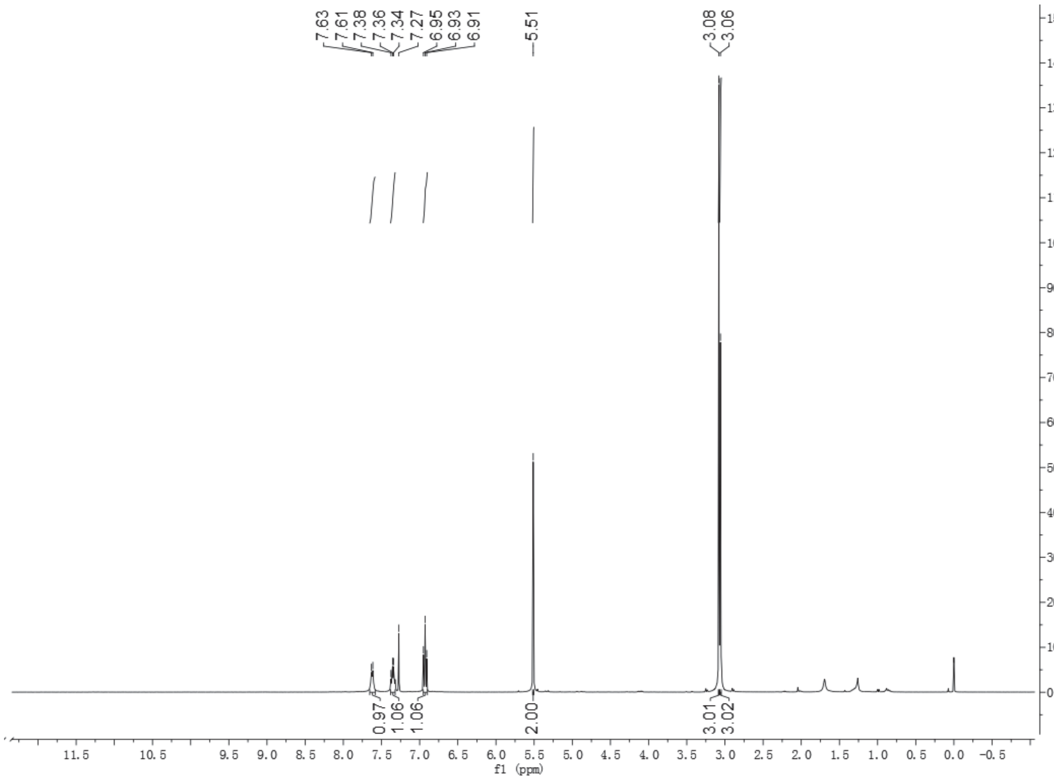
3a

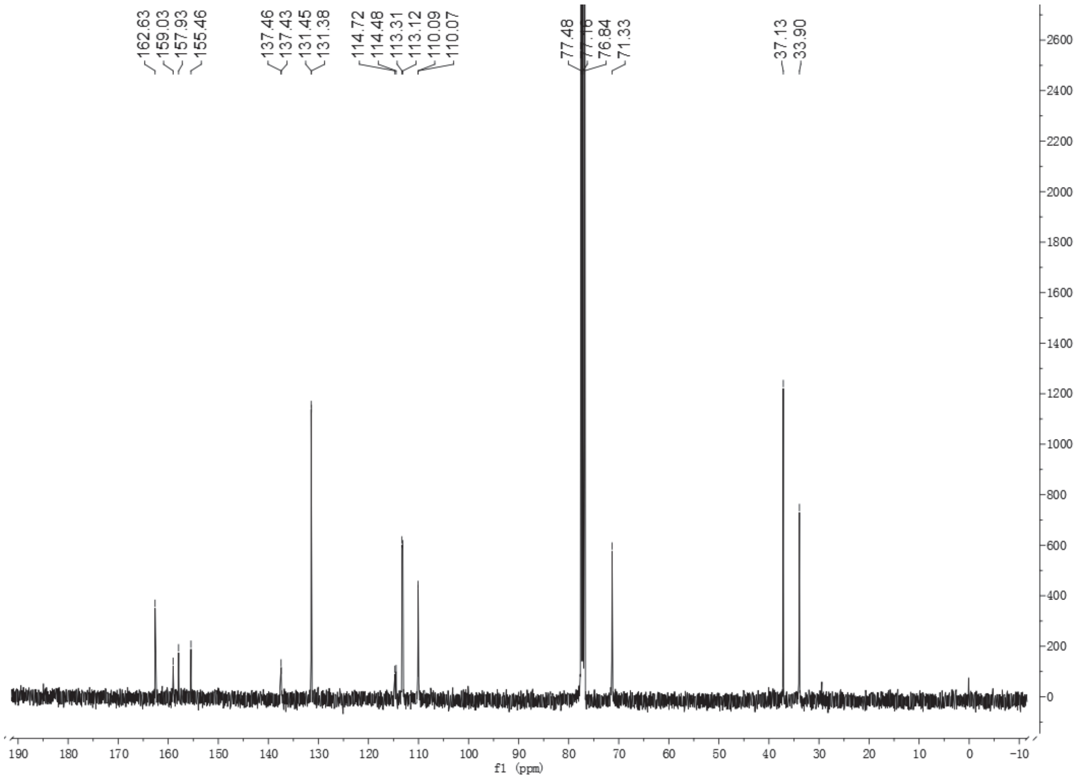

7.86
7.84
7.37
7.36
7.34
7.27
7.25
7.24
7.22
7.20
5.47
3.08
3.06
0.89
1.05
2.01
2.00
3.02
2.89
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
38000
36000
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000

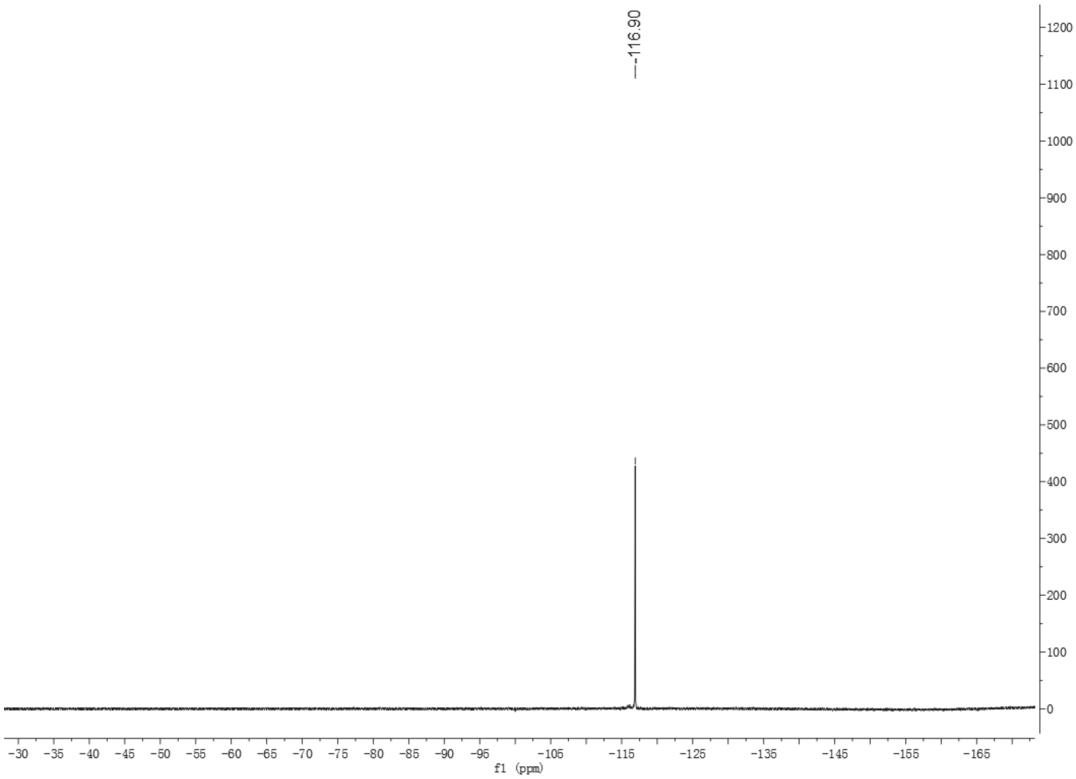

162.94
158.69
134.99
128.96
127.88
126.20
121.65
114.18
77.48
77.16
76.84
73.51
37.09
33.80
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
550
500
450
400
350
300
250
200
150
100
50
0

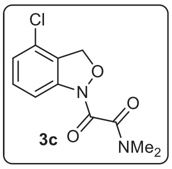

F
O
N
O
O
NMe2

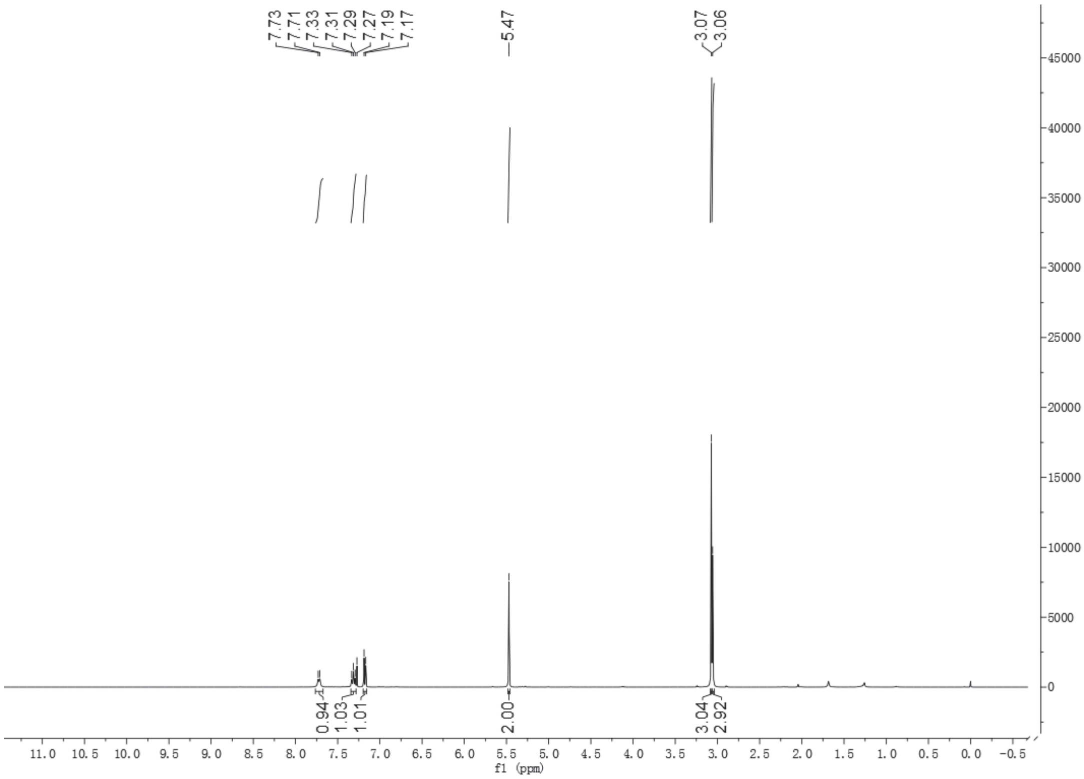
3b

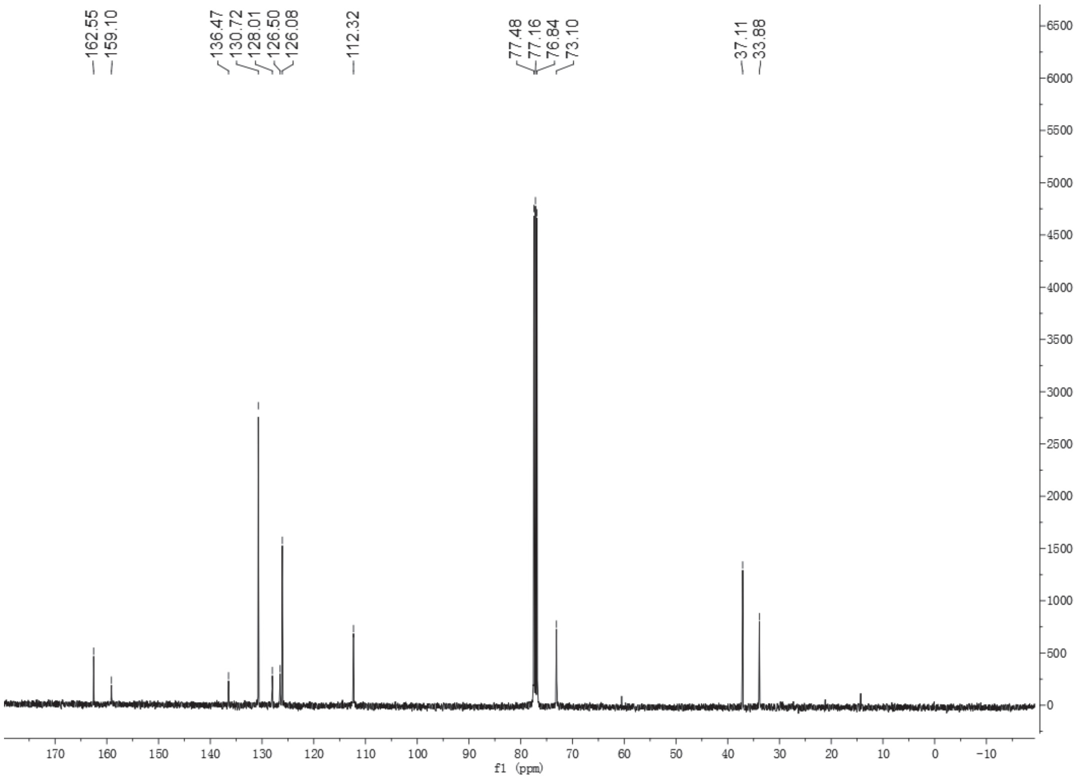

7.63
7.61
7.38
7.36
7.34
7.27
6.95
6.93
6.91
5.51
3.08
3.06
0.97
1.06
1.06
2.00
3.01
3.02
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0


162.63
159.03
157.93
155.46
137.46
137.43
131.45
131.38
114.72
114.48
113.31
113.12
110.09
110.07
77.48
77.16
76.84
71.33
37.13
33.90
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0

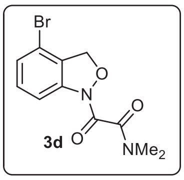

-116.90
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145 -155 -165
f1 (ppm)


Cl
O
N
O
O
NMe$_2$
3c


7.73
7.71
7.33
7.31
7.29
7.27
7.19
7.17
5.47
3.07
3.06
0.94
1.03
1.01
2.00
3.04
2.92
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

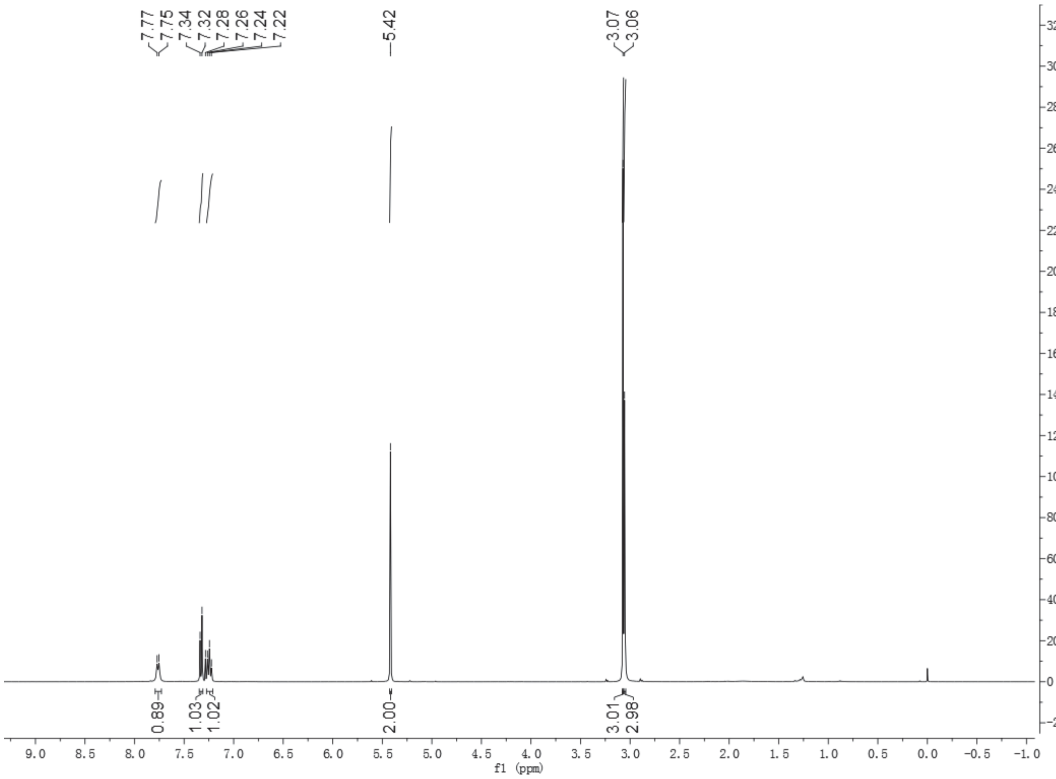


162.55
159.10
136.47
130.72
128.01
126.50
126.08
112.32
77.48
77.16
76.84
73.10
37.11
33.88
f1 (ppm)

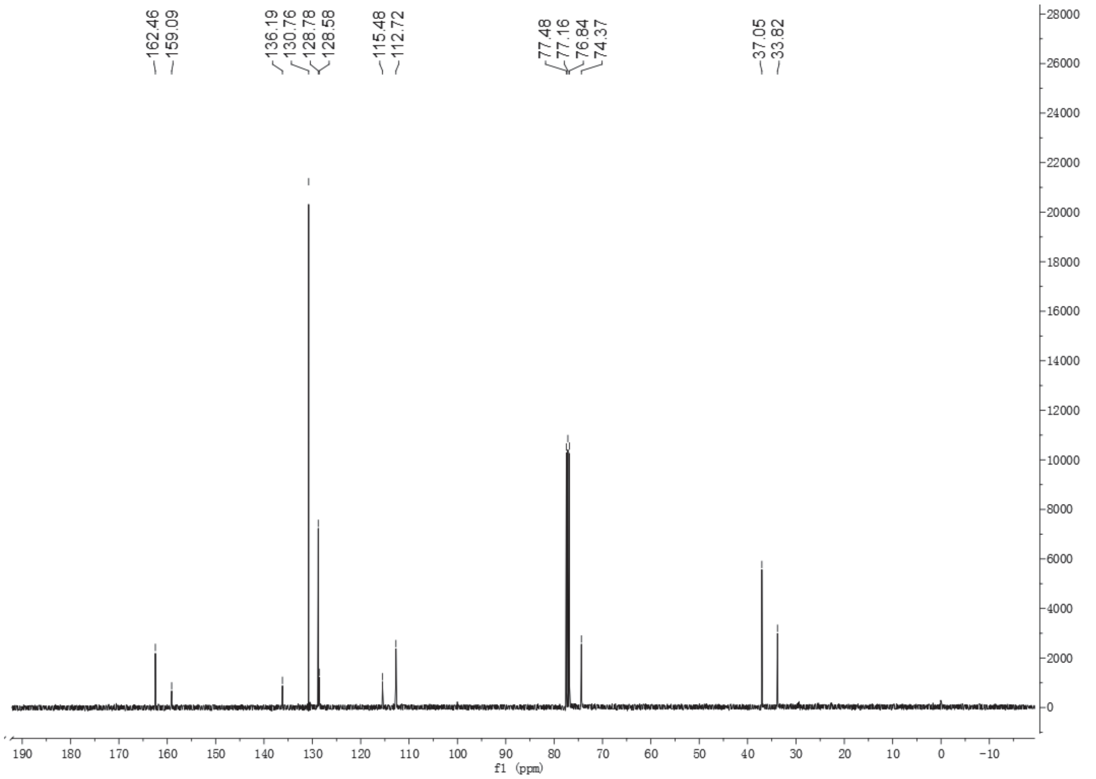


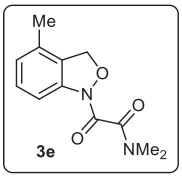
Br
O
N
O
O
NMe$_2$

3d

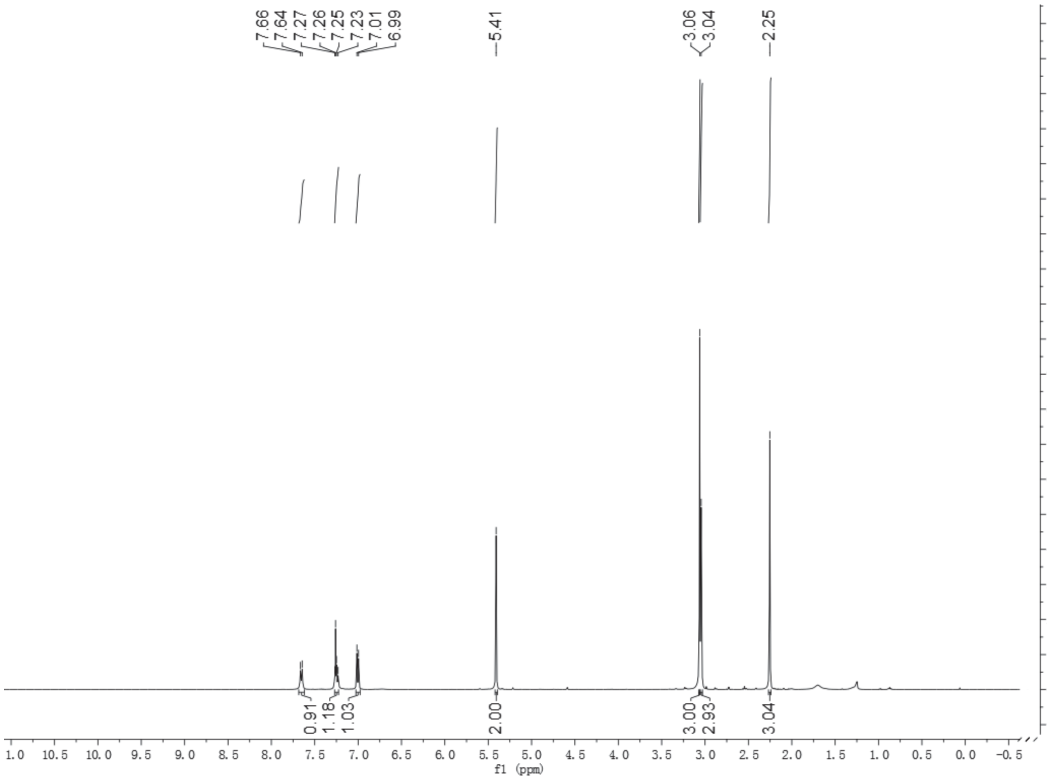


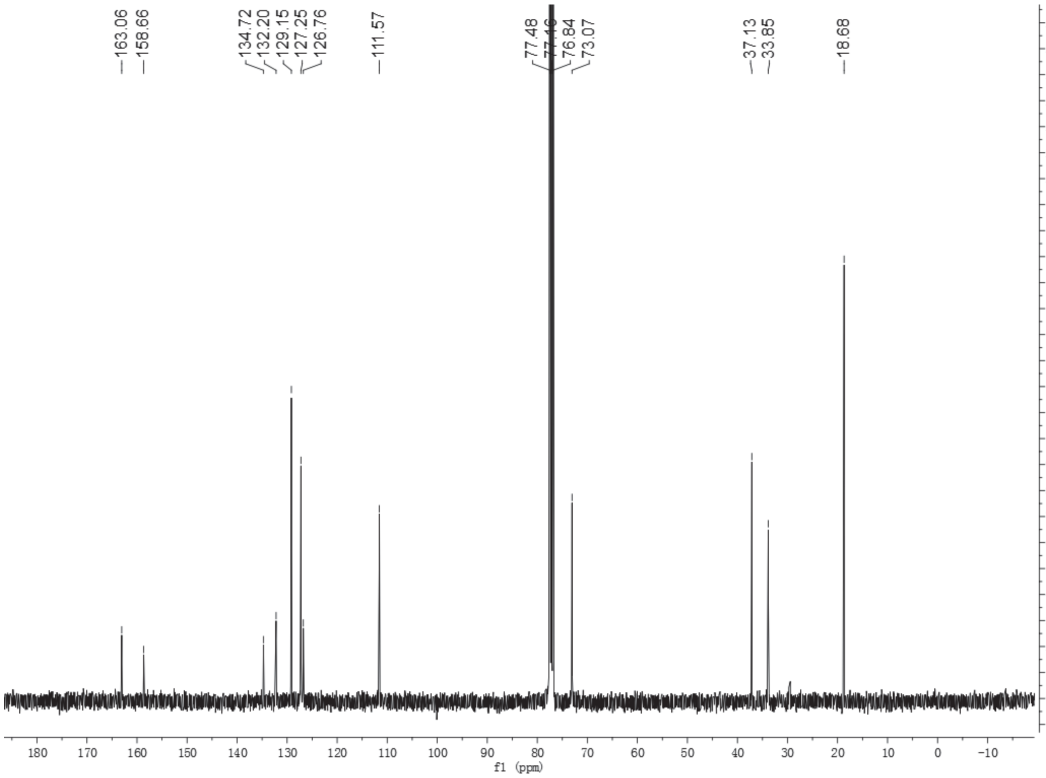
7.77
7.75
7.34
7.32
7.28
7.26
7.24
7.22
5.42
3.07
3.06
0.89
1.03
1.02
2.00
3.01
2.98
f1 (ppm)

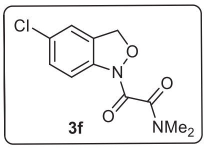

162.46
159.09
136.19
130.76
128.78
128.58
115.48
112.72
77.48
77.16
76.84
74.37
37.05
33.82
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Me
O
N
O
O
NMe2

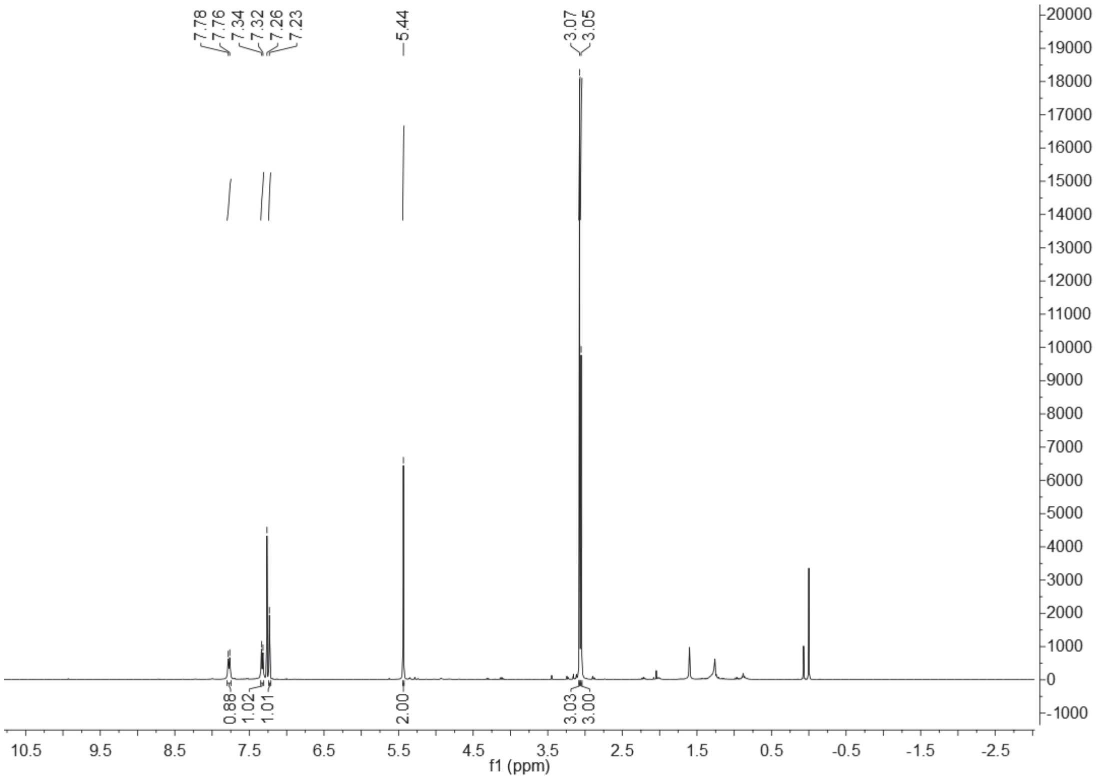
3e

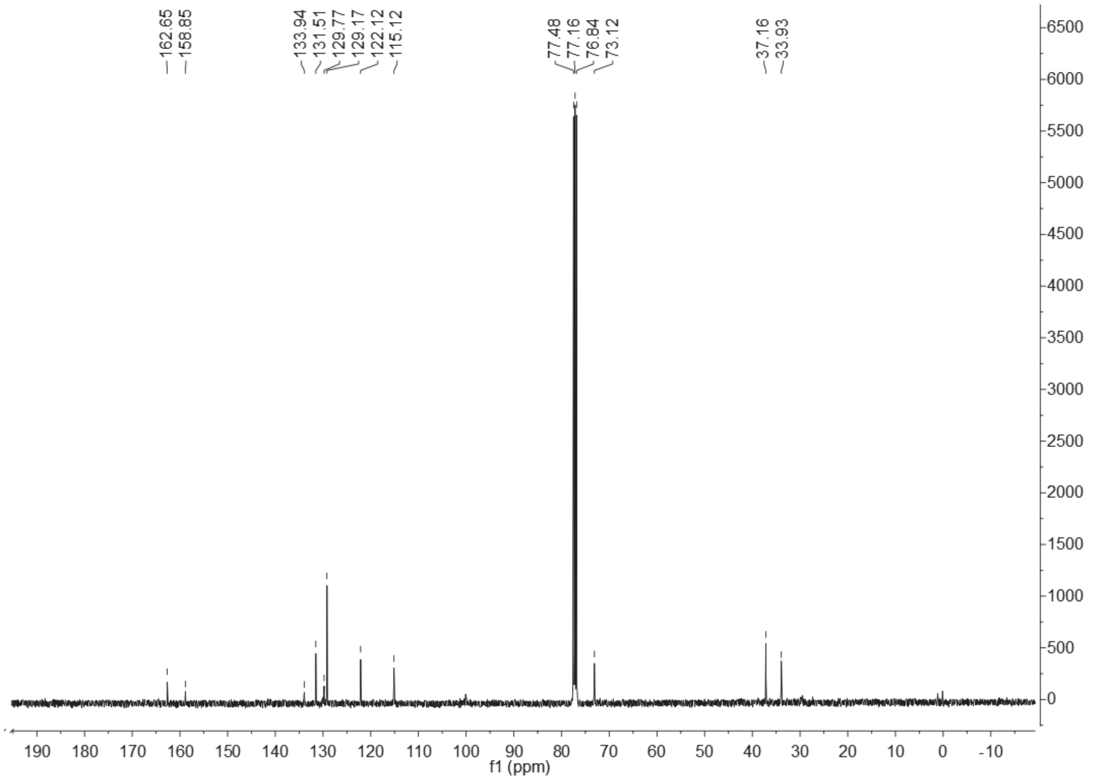

7.66
7.64
7.27
7.26
7.25
7.23
7.01
6.99
5.41
3.06
3.04
2.25
0.91
1.18
1.03
2.00
3.00
2.93
3.04
f1 (ppm)

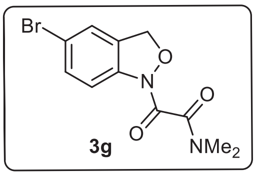

163.06
158.66
134.72
132.20
129.15
127.25
126.76
111.57
77.48
77.16
76.84
73.07
37.13
33.85
18.68
f1 (ppm)


Cl
O
N
O
O
NMe$_2$

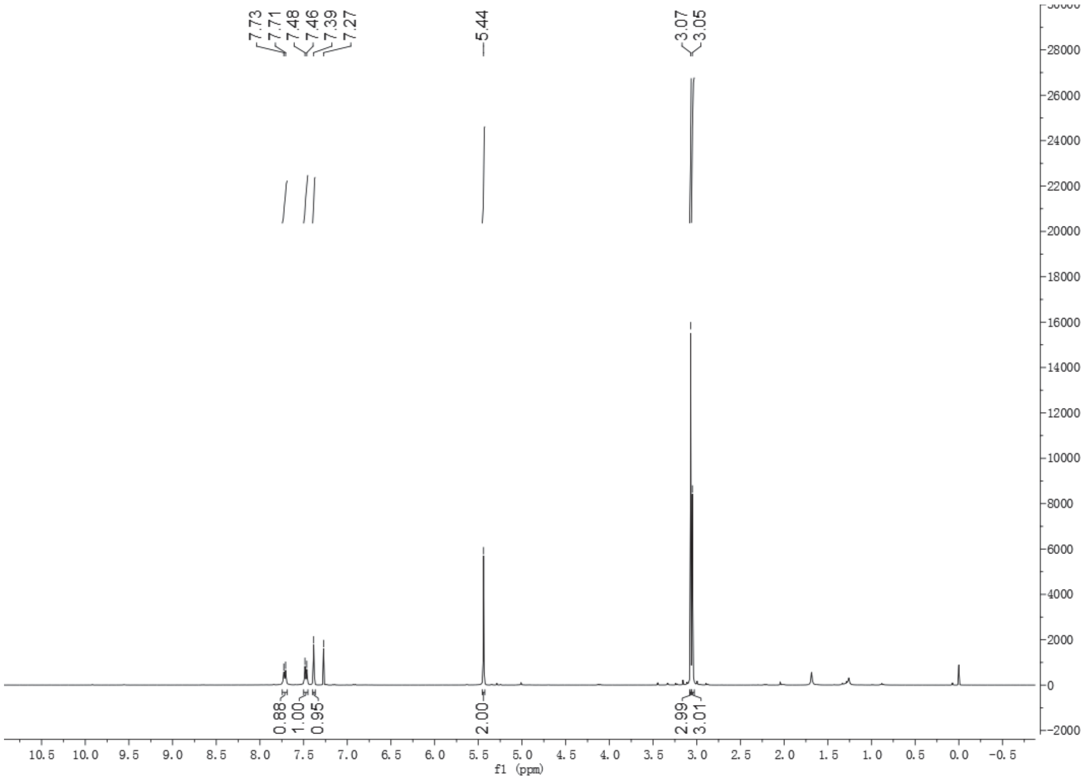
3f

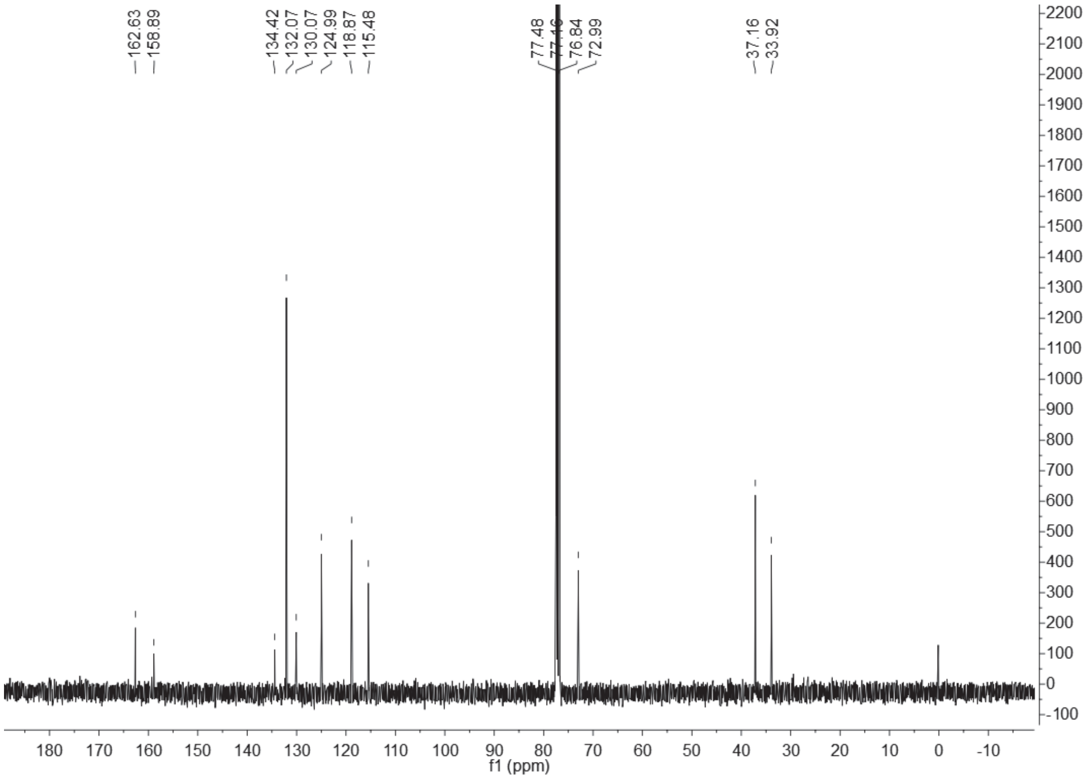

7.78
7.76
7.34
7.32
7.26
7.23
5.44
3.07
3.05
0.88
1.02
1.01
2.00
3.03
3.00
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
-2.5
f1 (ppm)

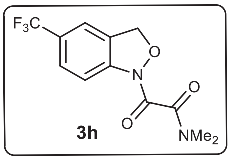

162.65
158.85
133.94
131.51
129.77
129.17
122.12
115.12
77.48
77.16
76.84
73.12
37.16
33.93
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Br
O
N
O
O
NMe2

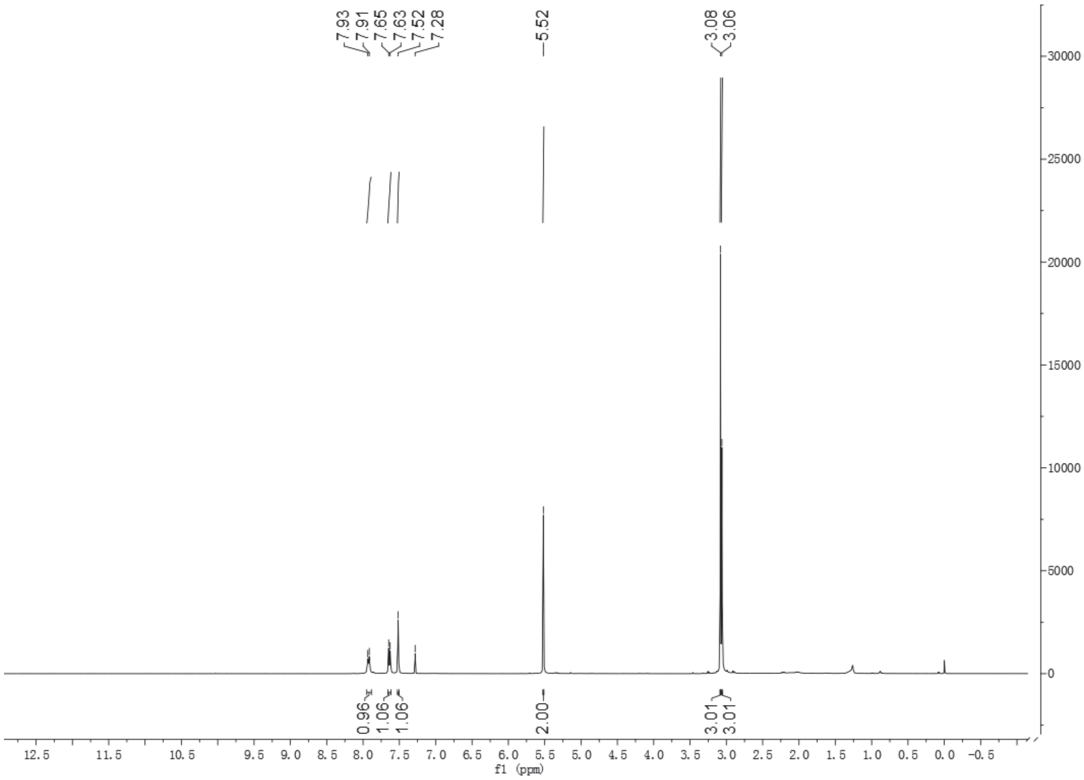
3g

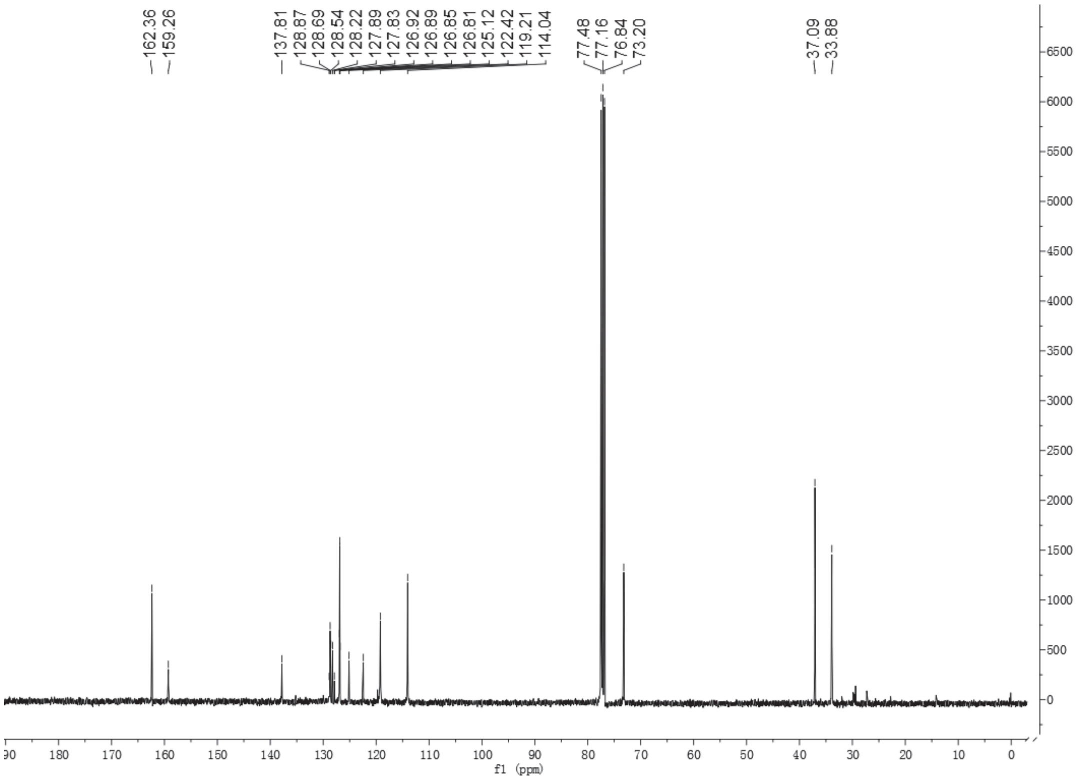

7.73
7.71
7.48
7.46
7.39
7.27
5.44
3.07
3.05
0.88
1.00
0.95
2.00
2.99
3.01
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

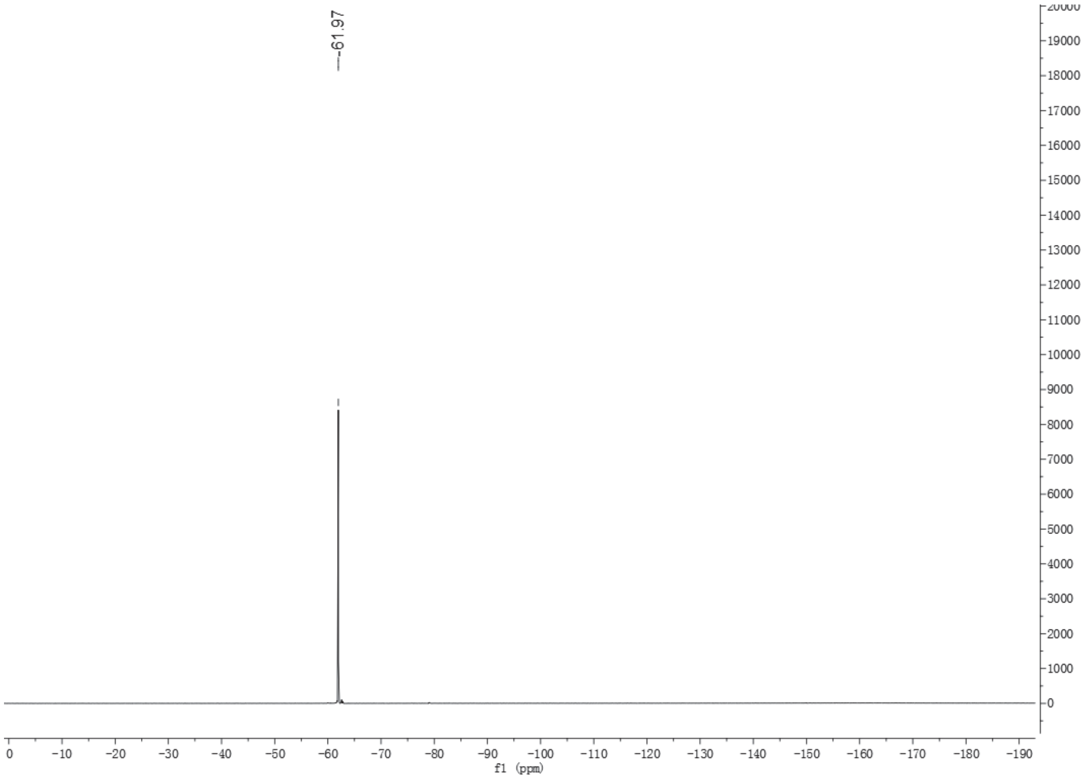

162.63
158.89
134.42
132.07
130.07
124.99
118.87
115.48
77.48
77.16
76.84
72.99
37.16
33.92
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


F3C
O
N
O
O
NMe2

3h


7.93
7.91
7.65
7.63
7.52
7.28
5.52
3.08
3.06
0.96
1.06
1.06
2.00
3.01
3.01
30000
25000
20000
15000
10000
5000
0
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


162.36
159.26
137.81
128.87
128.69
128.54
128.22
127.89
127.83
126.92
126.89
126.85
126.81
125.12
122.42
119.21
114.04
77.48
77.16
76.84
73.20
37.09
33.88
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



-61.97
f1 (ppm)
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
20000
19000
18000
17000
16000
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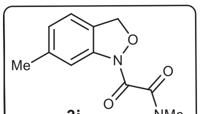
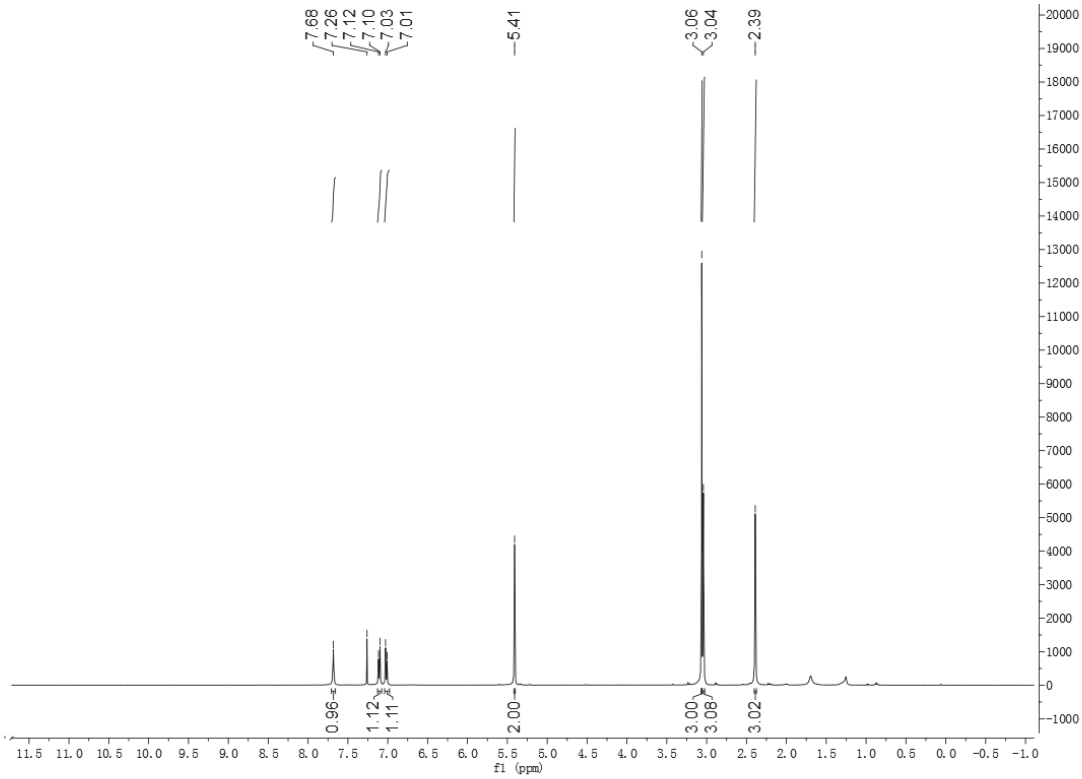
5000
4000
3000
2000
1000
0

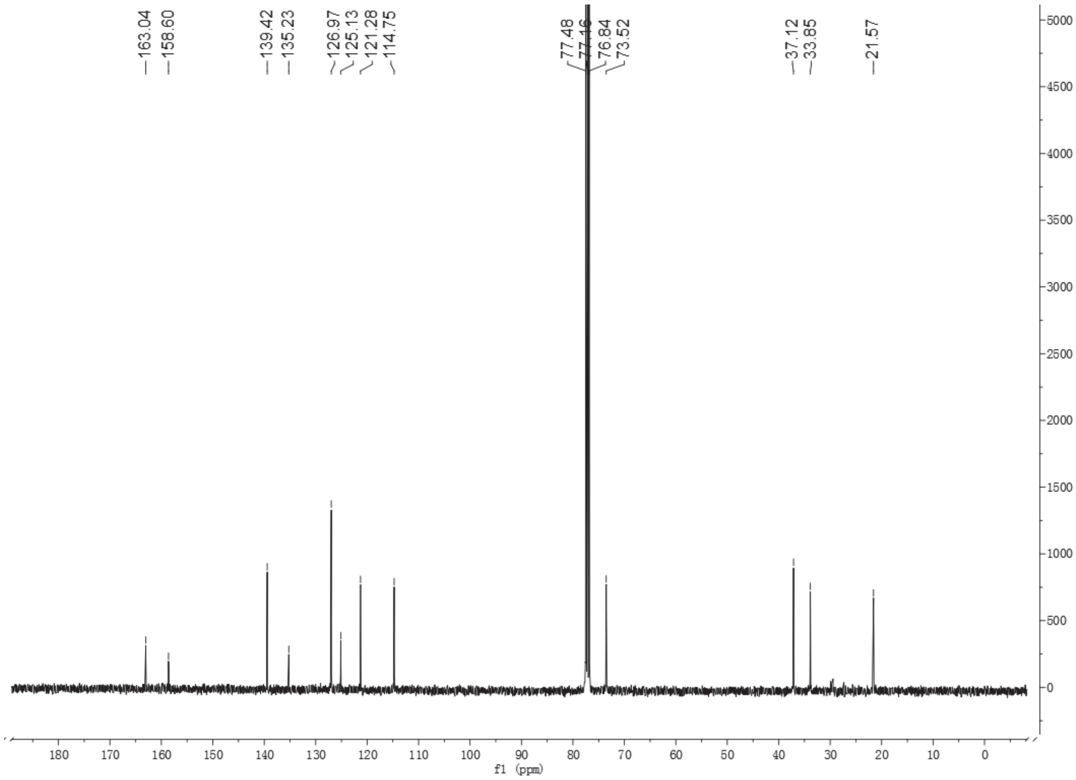


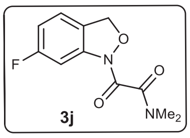
Me
N
O
O
O
NMe$_2$

3i

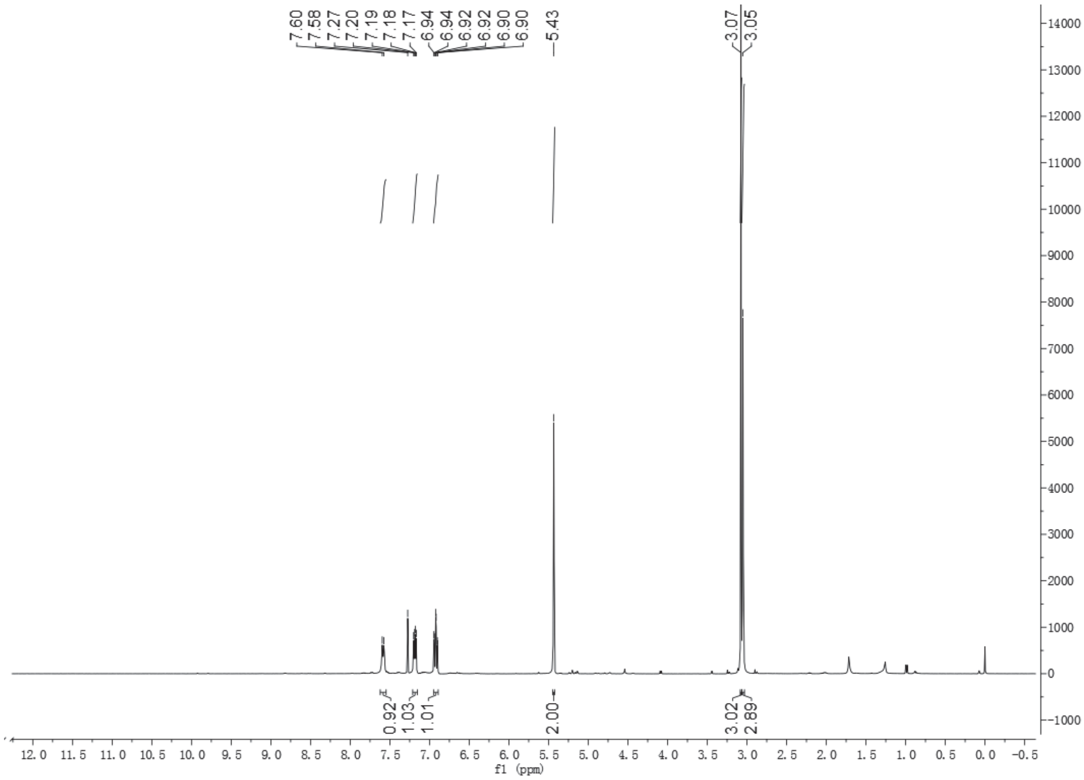


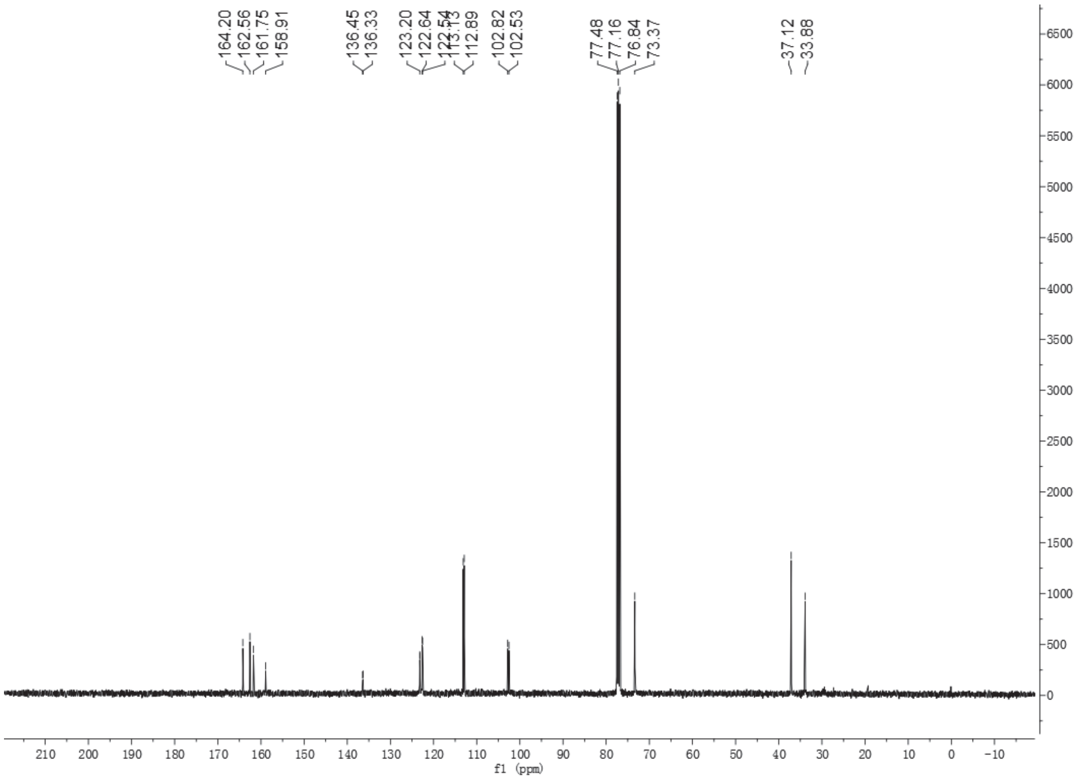
7.68
7.26
7.12
7.10
7.03
7.01
5.41
3.06
3.04
2.39
0.96
1.12
1.11
2.00
3.00
3.08
3.02
f1 (ppm)
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000

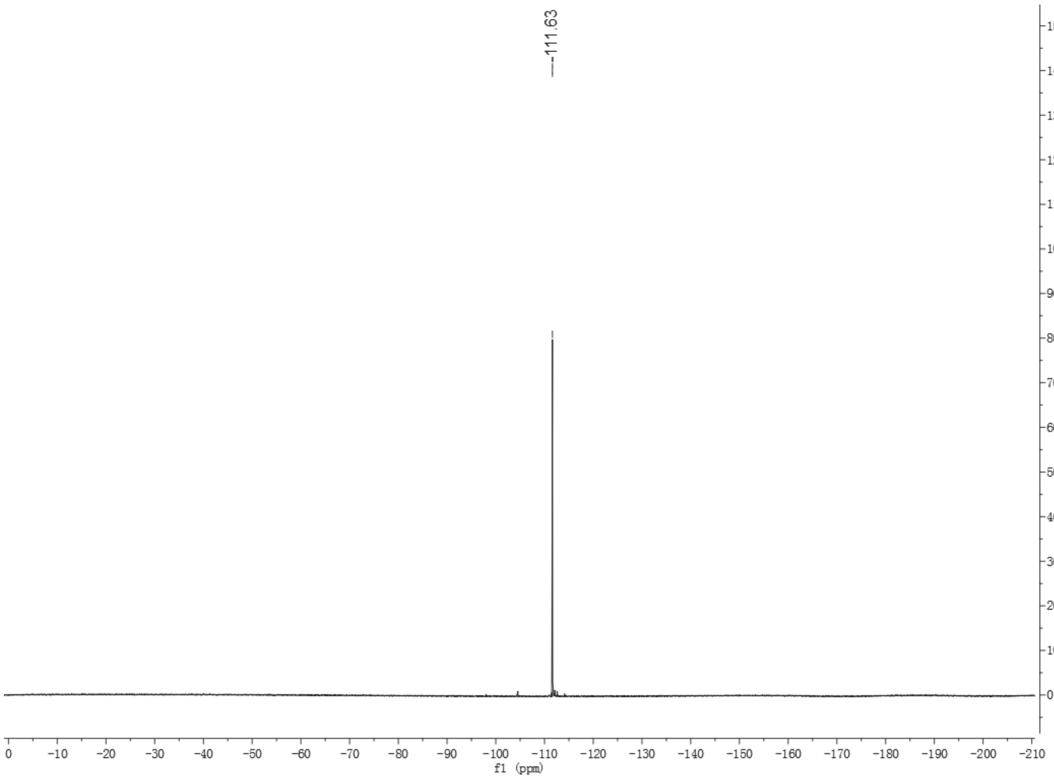

163.04
158.60
139.42
135.23
126.97
125.13
121.28
114.75
77.48
77.16
76.84
73.52
37.12
33.85
21.57
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

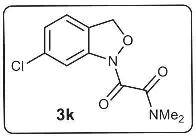

F
N
O
O
O
NMe$_2$

3j

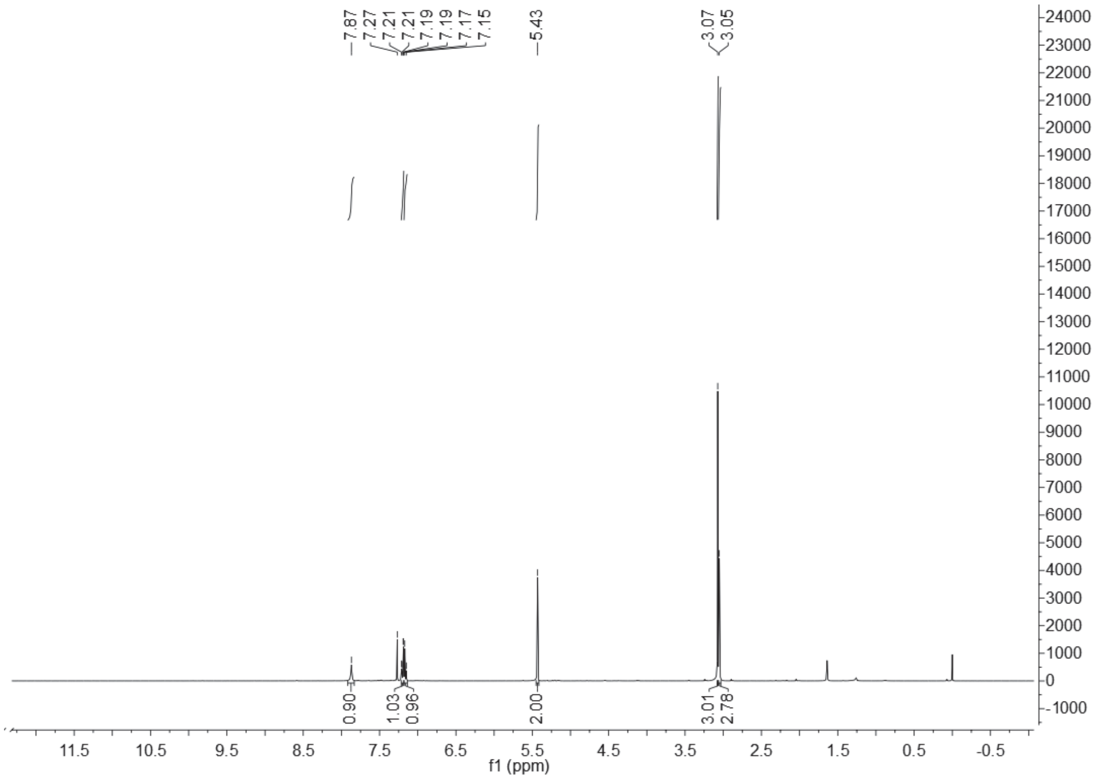

7.60
7.58
7.27
7.20
7.19
7.18
7.17
6.94
6.94
6.92
6.92
6.90
6.90
5.43
3.07
3.05
0.92
1.03
1.01
2.00
3.02
2.89
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

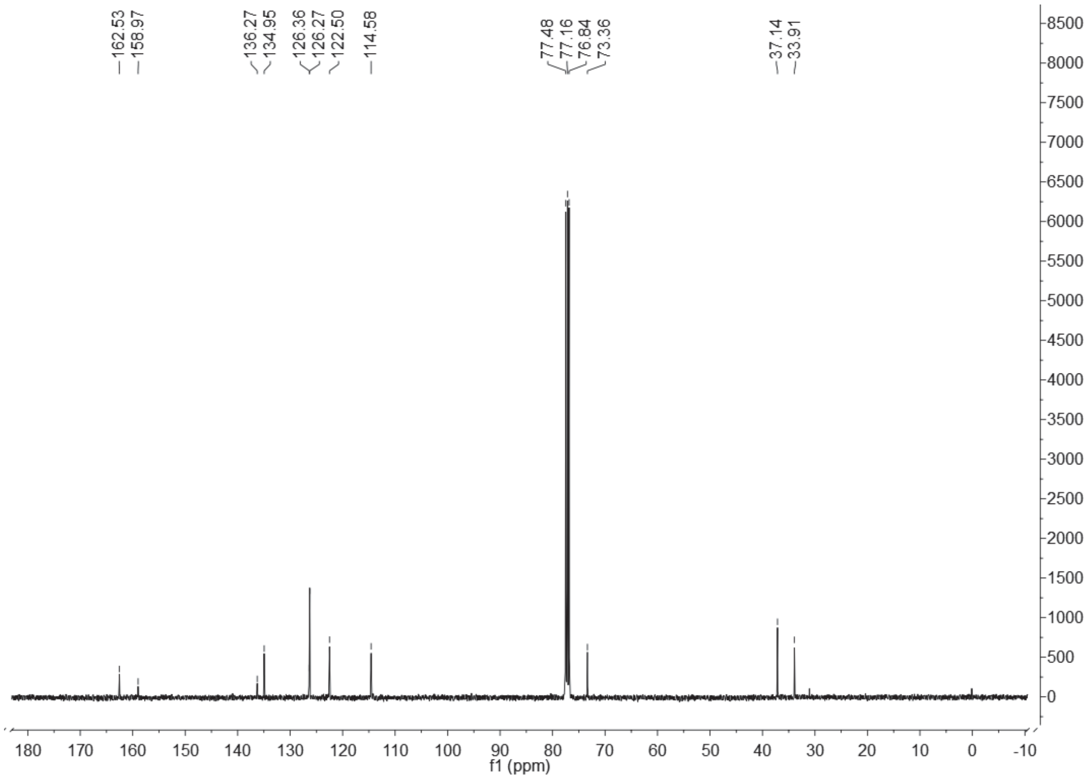

164.20
162.56
161.75
158.91
136.45
136.33
123.20
122.64
122.54
113.13
112.89
102.82
102.53
77.48
77.16
76.84
73.37
37.12
33.88
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

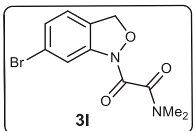

-111.63
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)


Cl
N
O
O
O
NMe$_2$

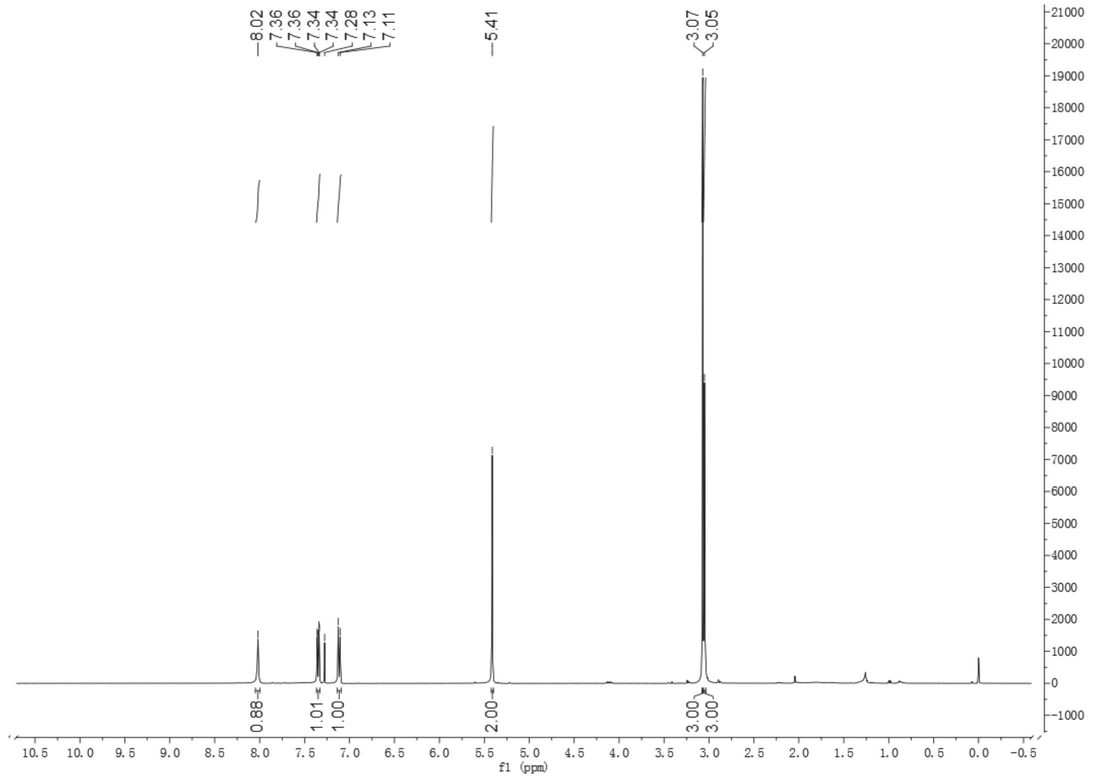
3k

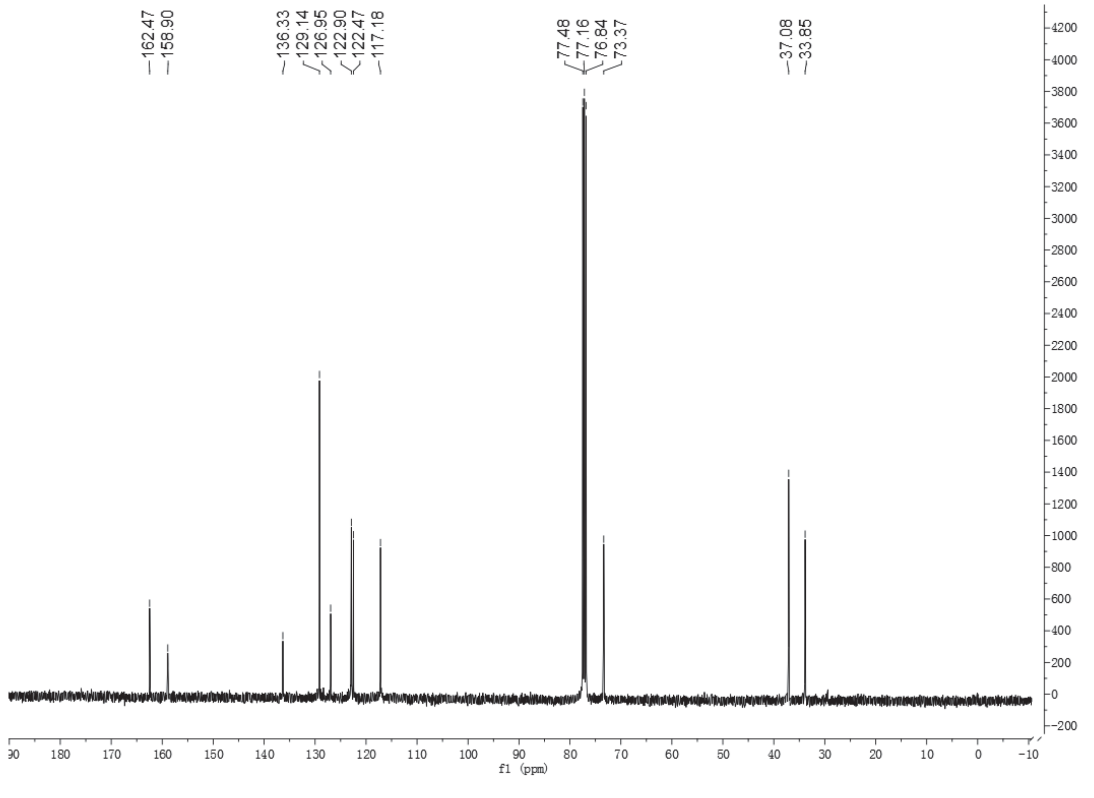

7.87
7.27
7.21
7.21
7.19
7.19
7.17
7.15
5.43
3.07
3.05
0.90
1.03
0.96
2.00
3.01
2.78
24000
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

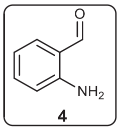

162.53
158.97
136.27
134.95
126.36
126.27
122.50
114.58
77.48
77.16
76.84
73.36
37.14
33.91
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Br
N
O
O
O
NMe$_2$

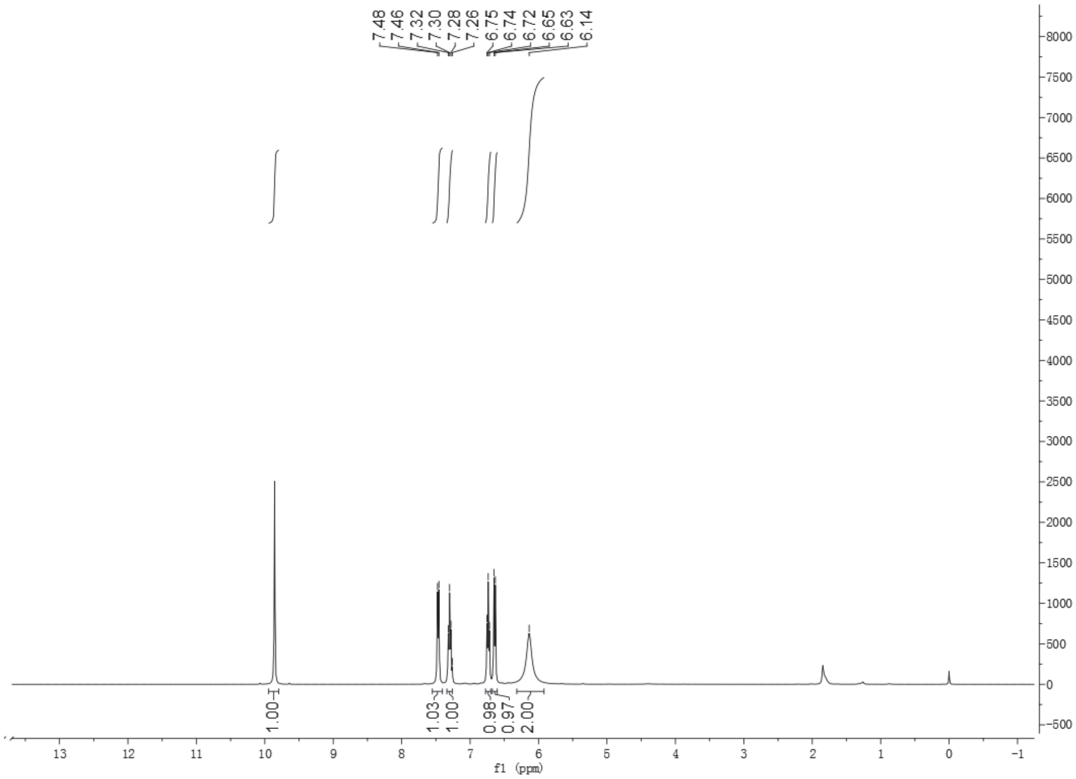
3l

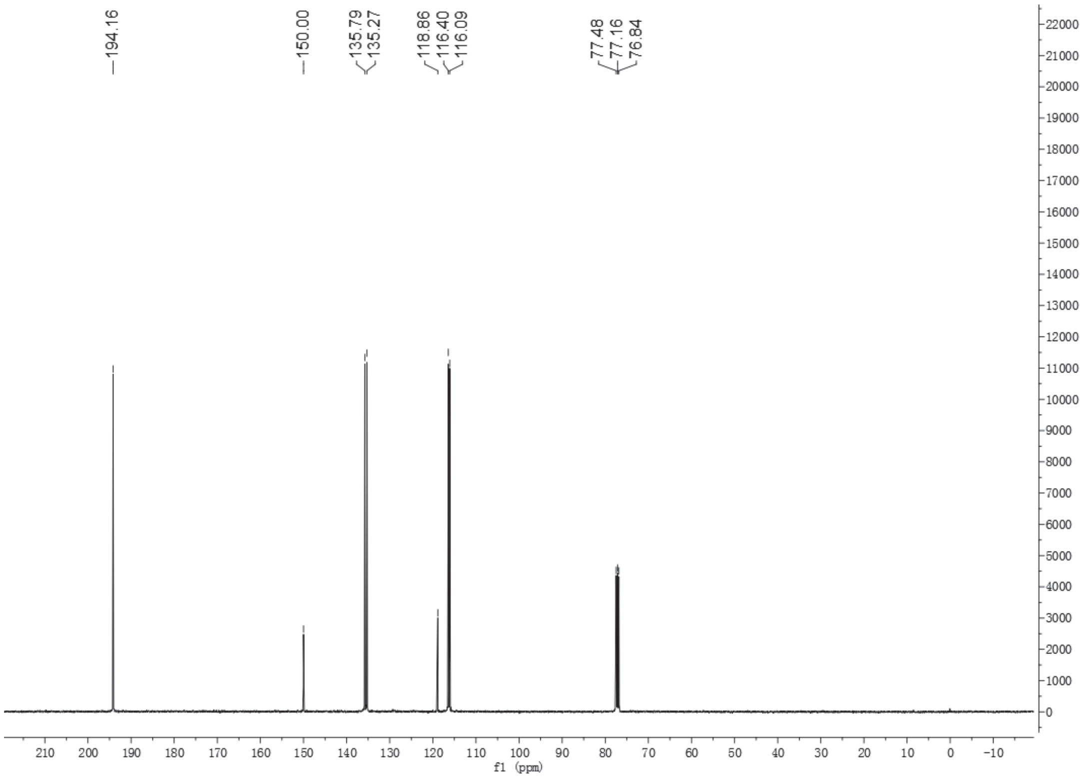

8.02
7.36
7.36
7.34
7.34
7.28
7.13
7.11
5.41
3.07
3.05
0.88
1.01
1.00
2.00
3.00
3.00
f1 (ppm)
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
21000 20000 19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 -1000

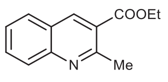

162.47
158.90
136.33
129.14
126.95
122.90
122.47
117.18
77.48
77.16
76.84
73.37
37.08
33.85
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
4200 4000 3800 3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200


O
NH2

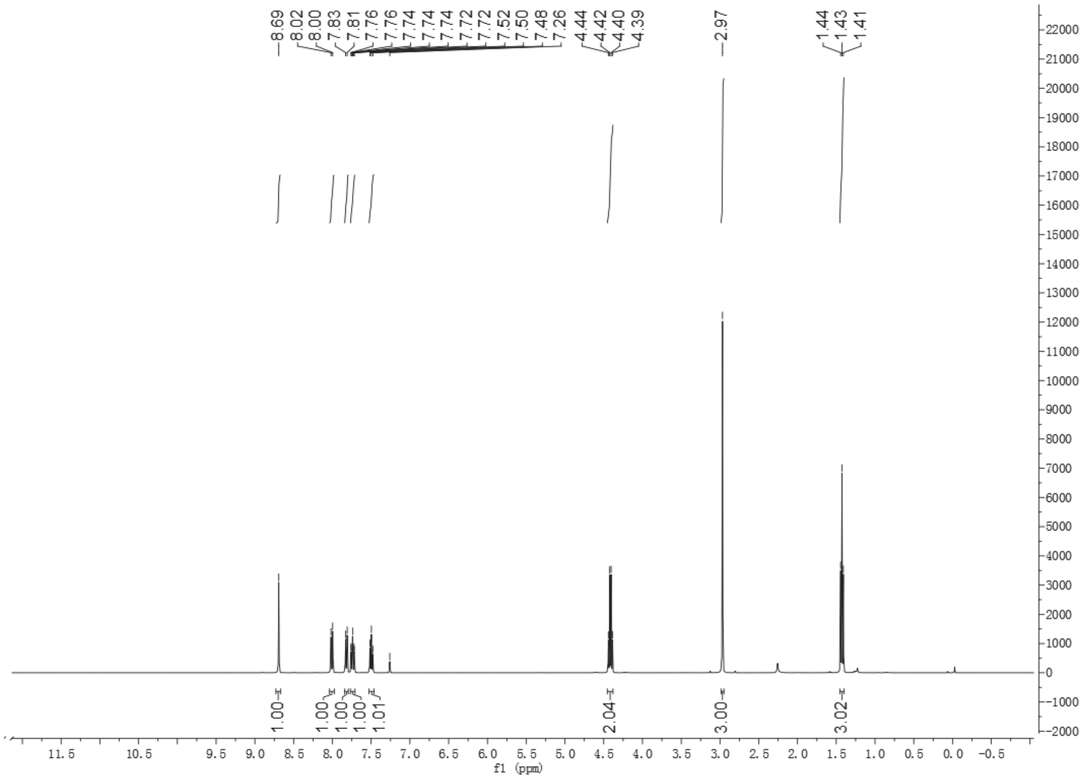
4

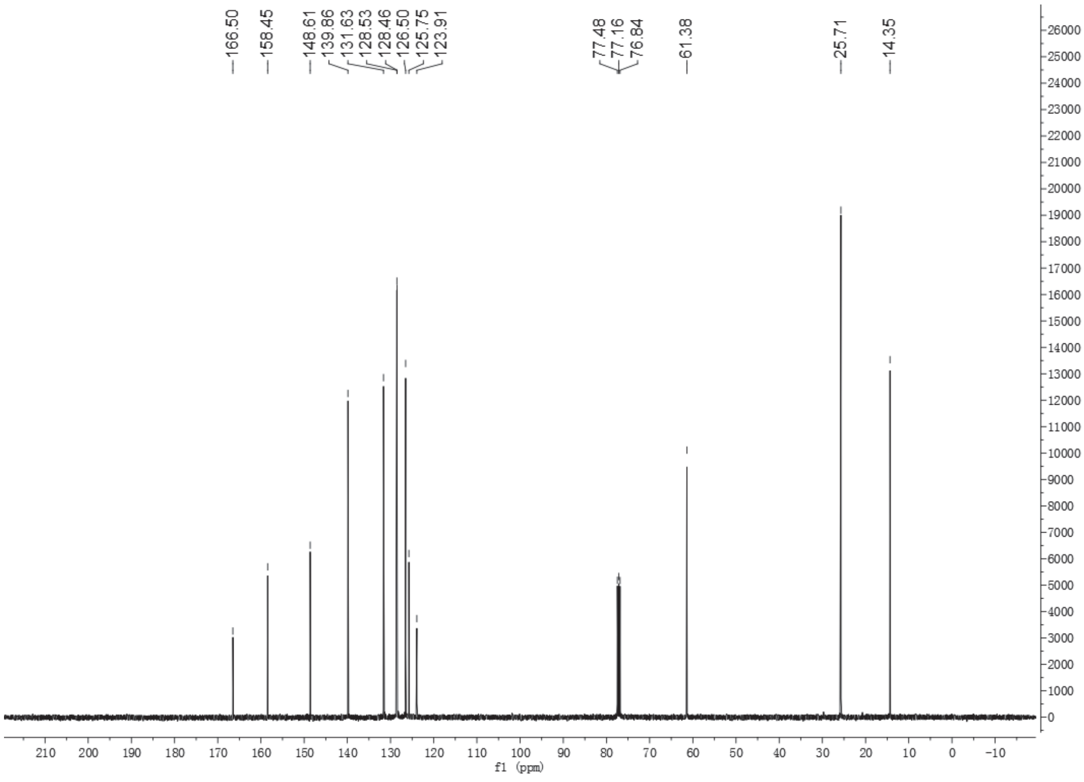

7.48
7.46
7.32
7.30
7.28
7.26
6.75
6.74
6.72
6.65
6.63
6.14
1.00
1.03
1.00
0.98
0.97
2.00
f1 (ppm)
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
−500


194.16
150.00
135.79
135.27
118.86
116.40
116.09
77.48
77.16
76.84
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0


COOEt
N
Me

5


8.69
8.02
8.00
7.83
7.81
7.76
7.74
7.74
7.74
7.72
7.72
7.52
7.50
7.48
7.26
4.44
4.42
4.40
4.39
2.97
1.44
1.43
1.41
1.00
1.00
1.00
1.00
1.01
2.04
3.00
3.02
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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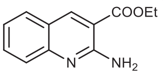
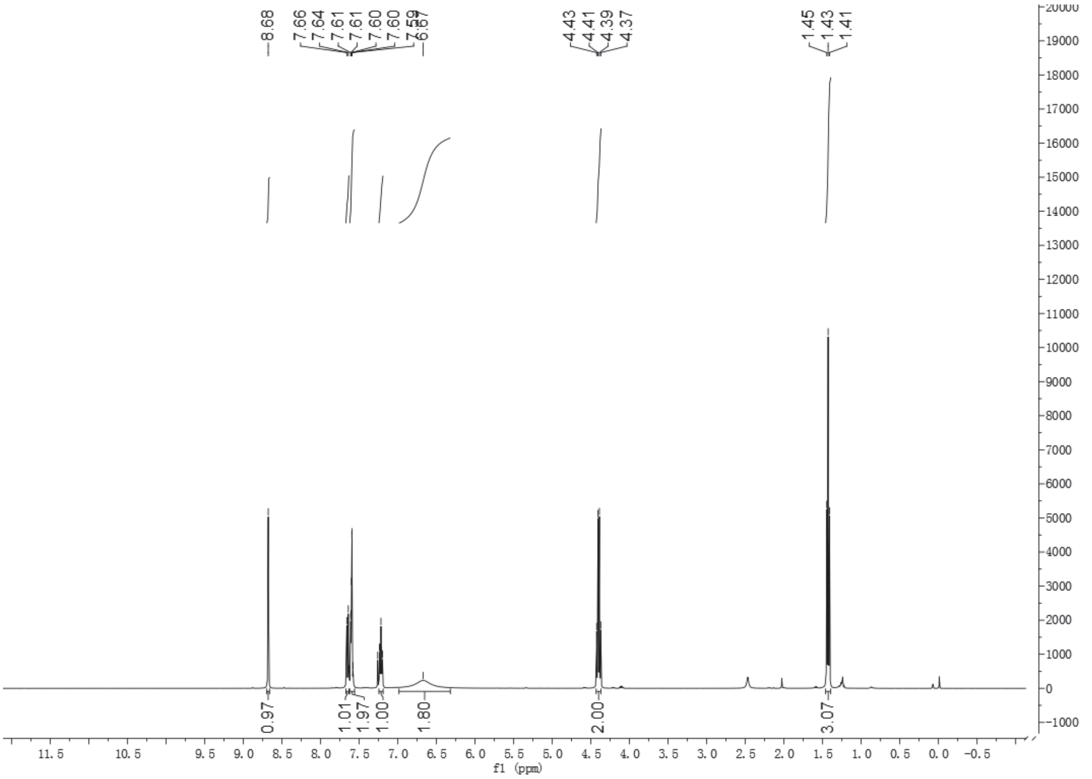
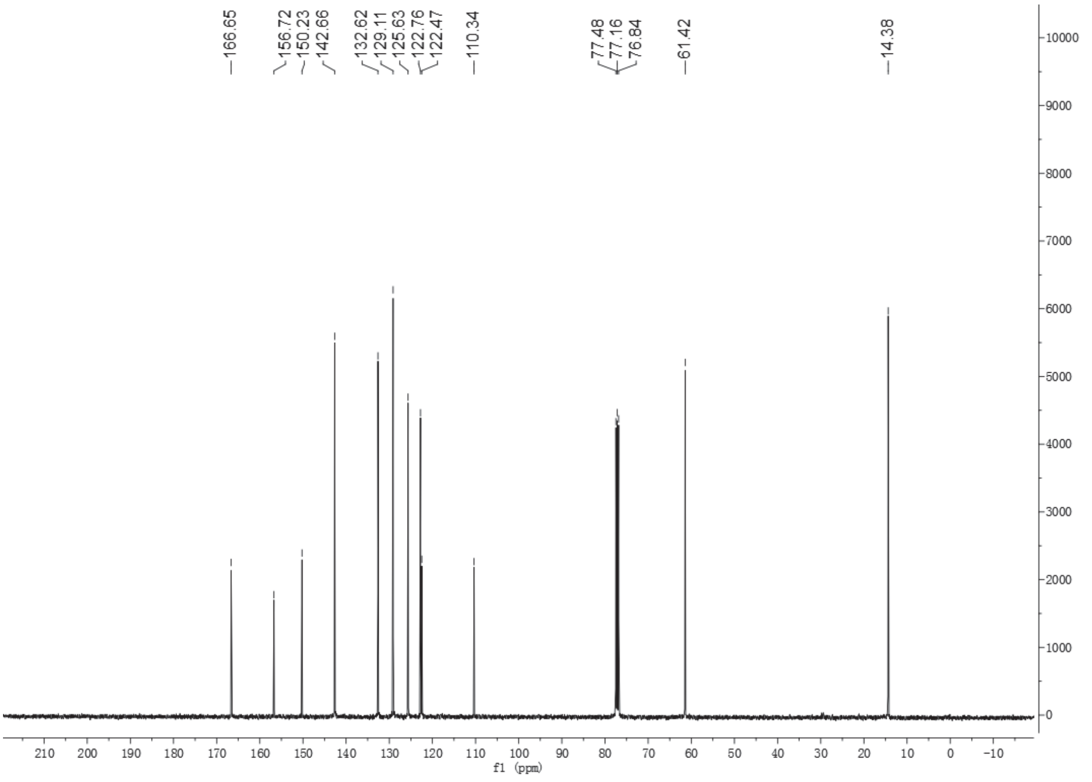
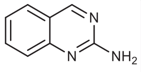
158.45
148.61
139.86
131.63
128.53
128.46
126.50
125.75
123.91
77.48
77.16
76.84
61.38
25.71
14.35
26000
25000
24000
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


COOEt
N
NH2

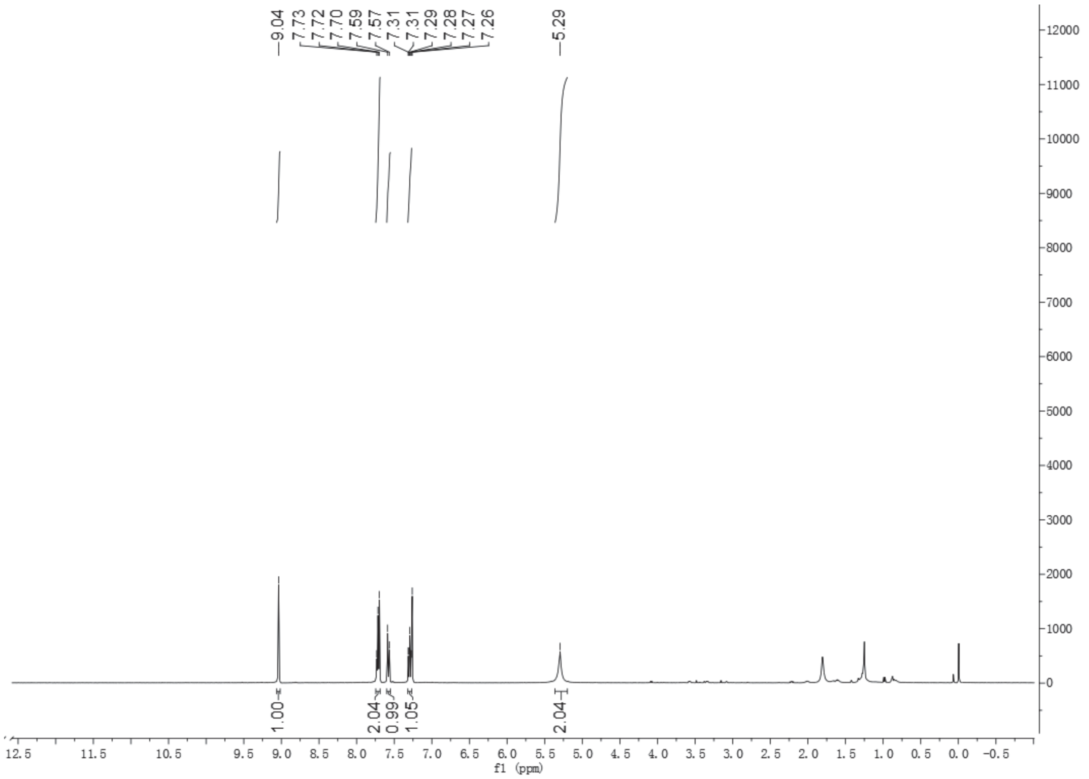
6

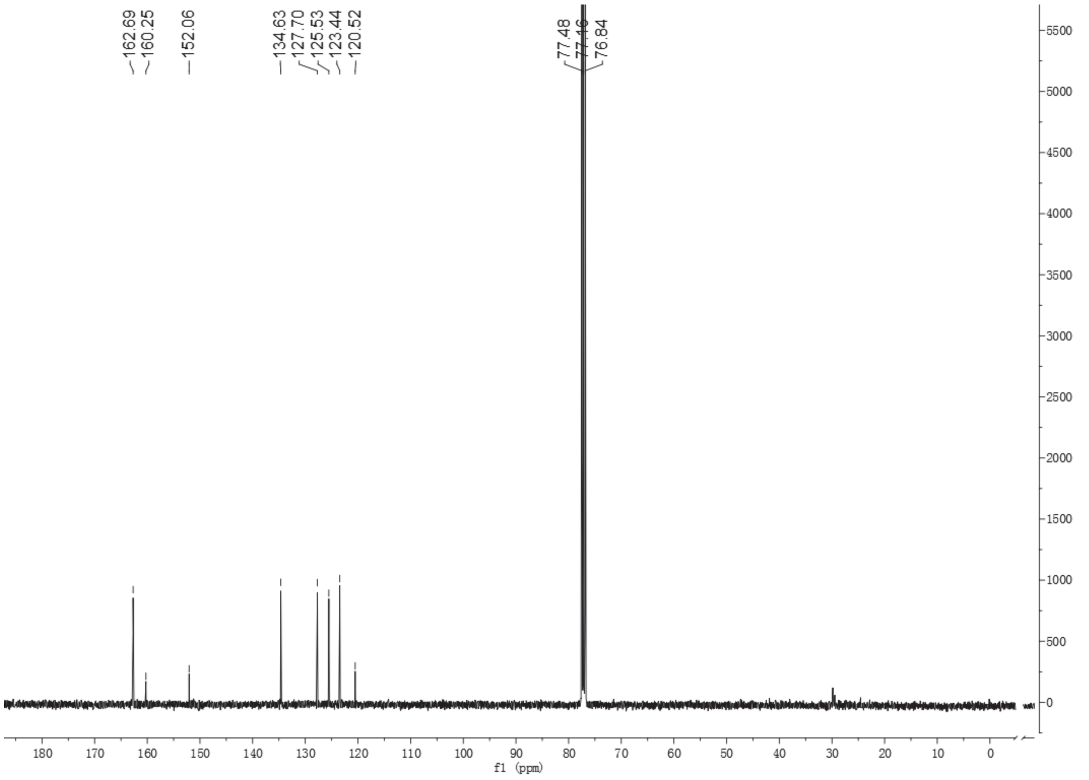

8.68
7.66
7.64
7.61
7.61
7.60
7.60
7.59
6.67
4.43
4.41
4.39
4.37
1.45
1.43
1.41
0.97
1.01
1.97
1.00
1.80
2.00
3.07
f1 (ppm)

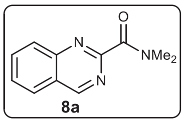

166.65
156.72
150.23
142.66
132.62
129.11
125.63
122.76
122.47
110.34
77.48
77.16
76.84
61.42
14.38
f1 (ppm)


N
N
NH2

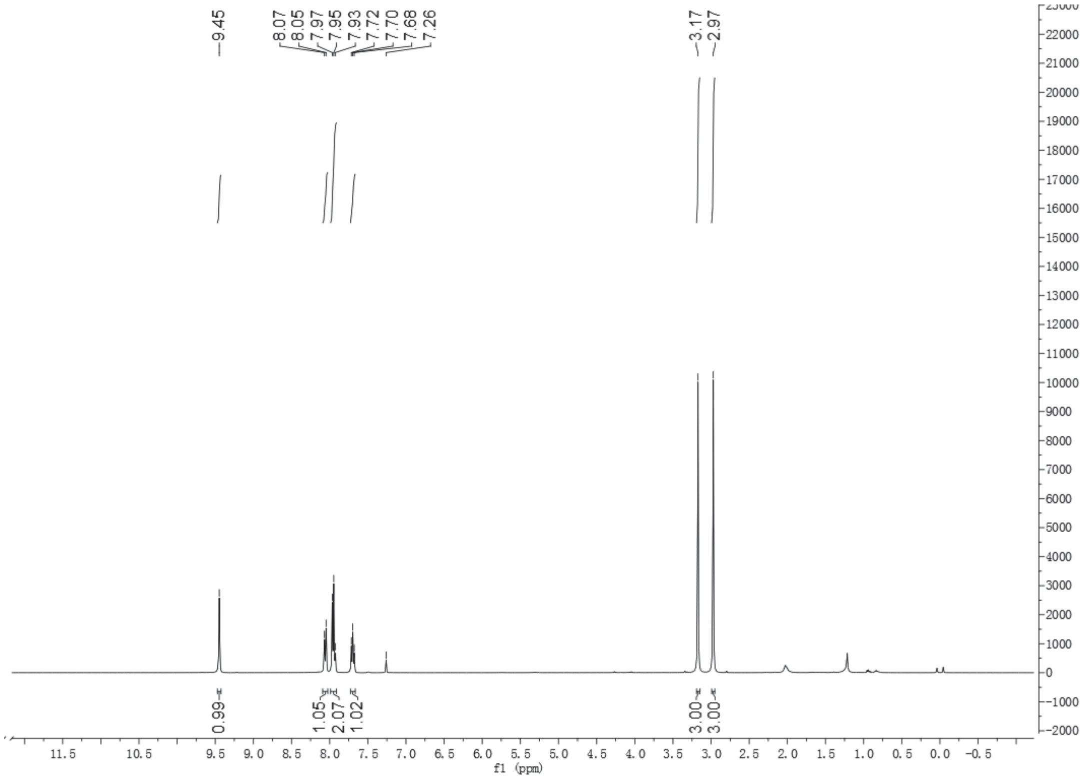
7

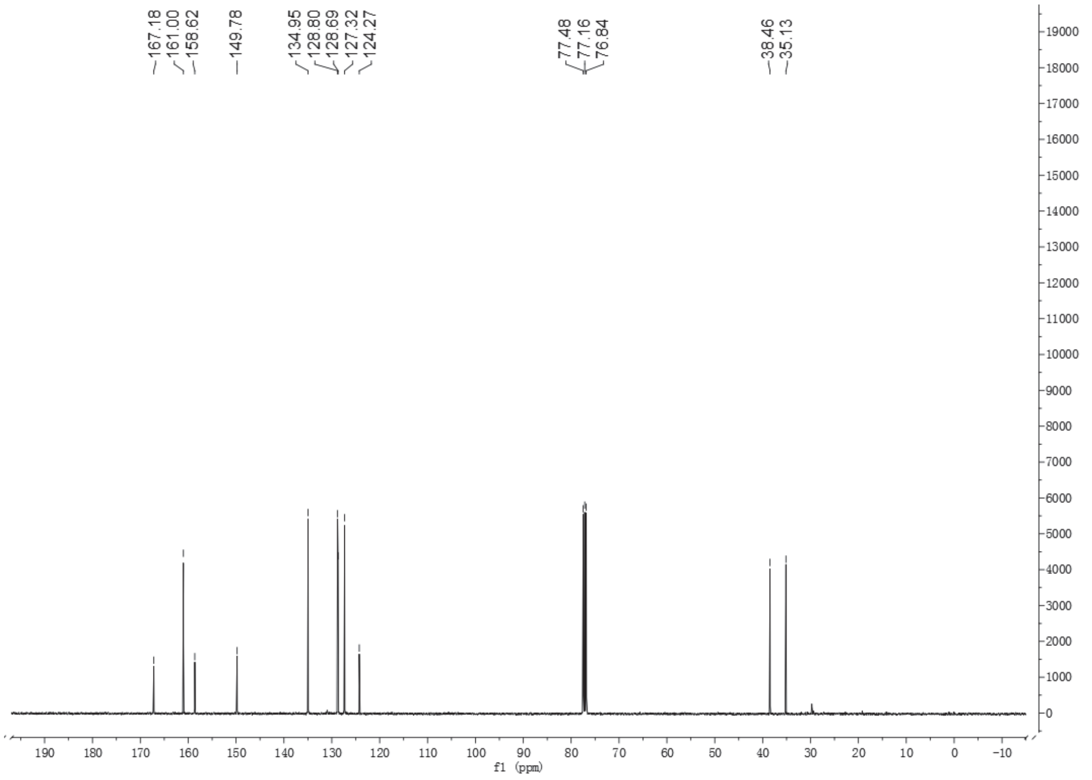

9.04
7.73
7.72
7.70
7.59
7.57
7.31
7.31
7.29
7.28
7.27
7.26
5.29
1.00
2.04
0.99
1.05
2.04
12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0

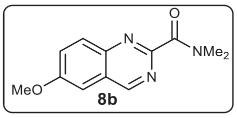

162.69
160.25
152.06
134.63
127.70
125.53
123.44
120.52
77.48
77.16
76.84
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0


O
N
N
NMe2

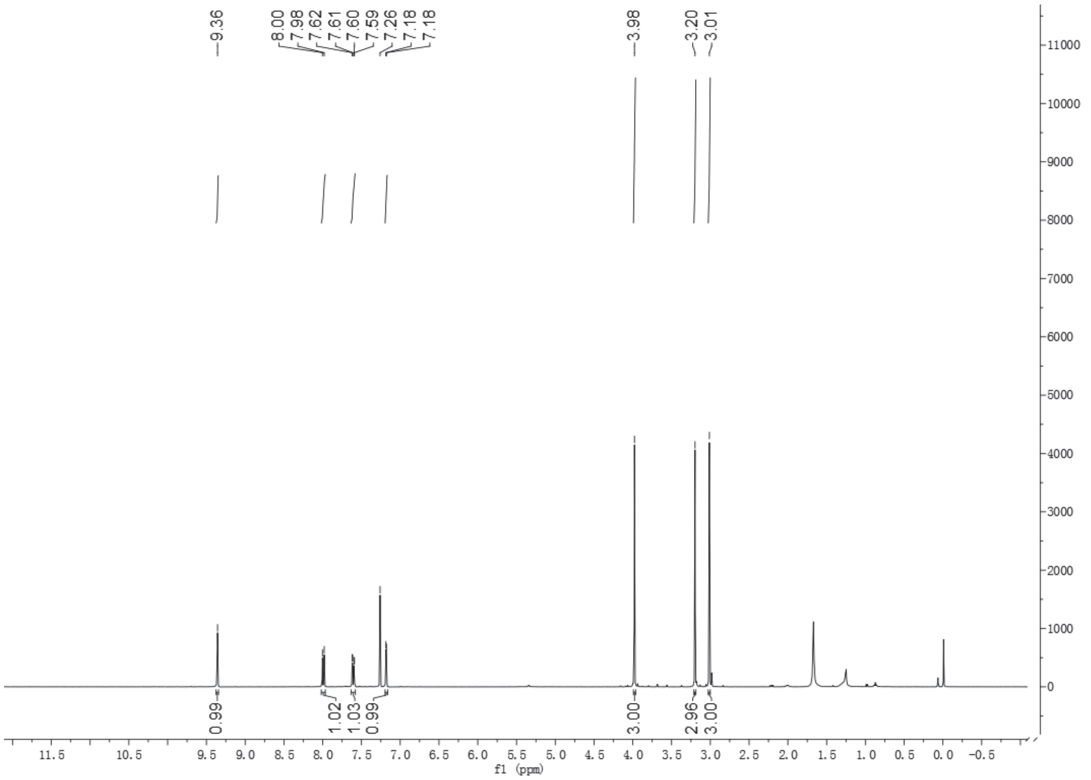
8a

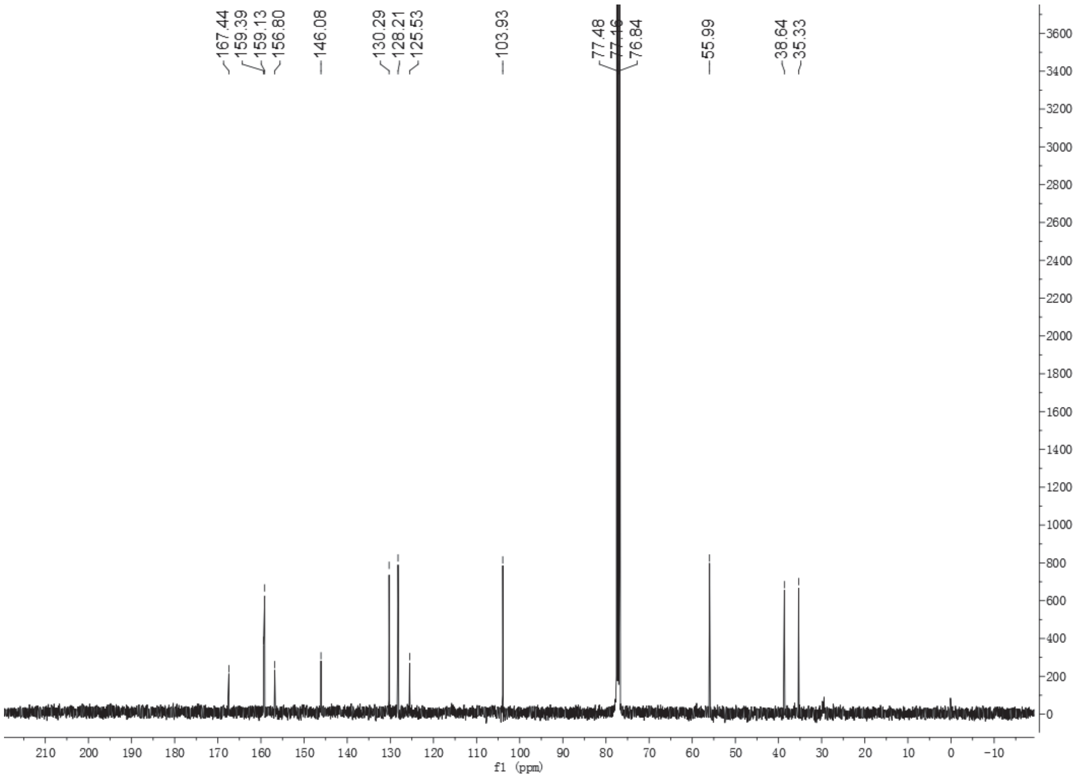

9.45
8.07
8.05
7.97
7.95
7.93
7.72
7.70
7.68
7.26
3.17
2.97
0.99
1.05
2.07
1.02
3.00
3.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000

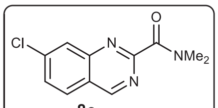

167.18
161.00
158.62
149.78
134.95
128.80
128.69
127.32
124.27
77.48
77.16
76.84
38.46
35.13
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0


NMe2
MeO
N
N
O

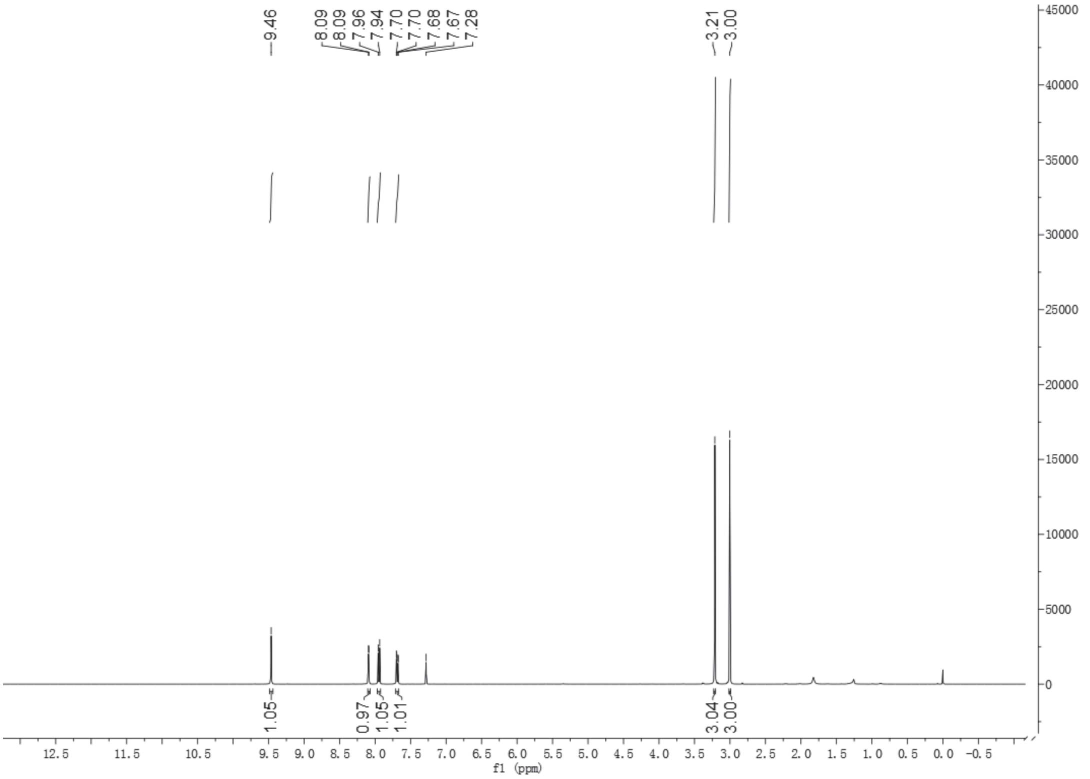
8b

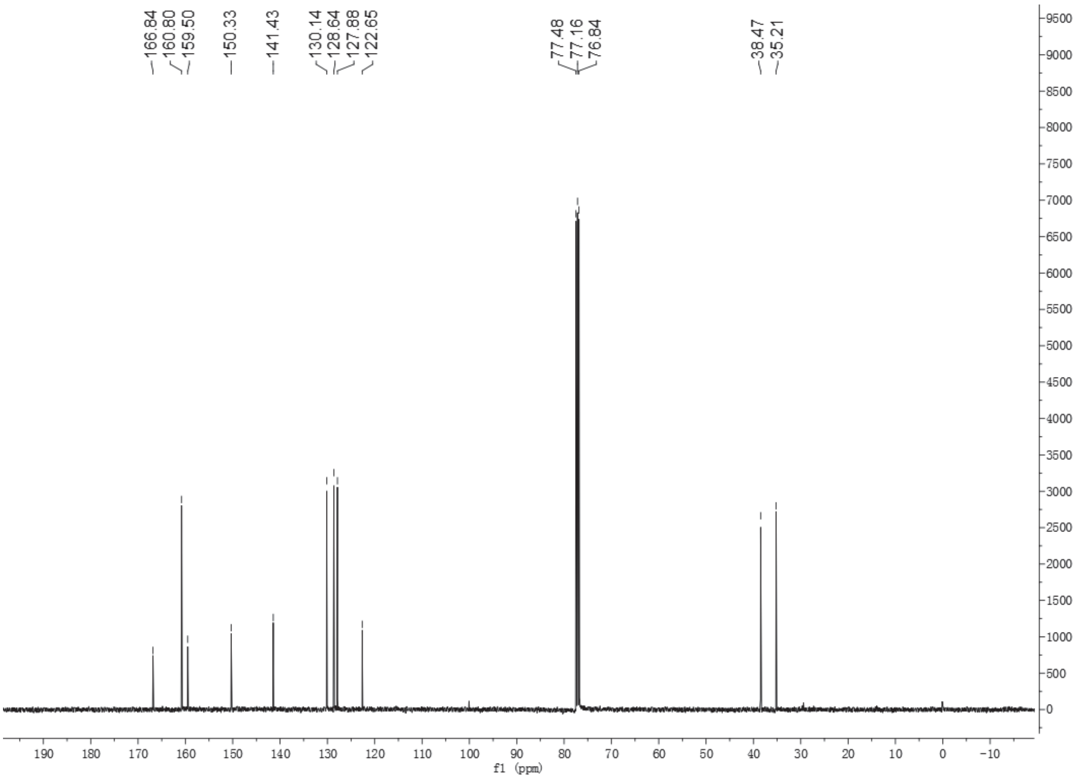

9.36
8.00
7.98
7.62
7.61
7.60
7.59
7.26
7.18
7.18
3.98
3.20
3.01
0.99
1.02
1.03
0.99
3.00
2.96
3.01
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0

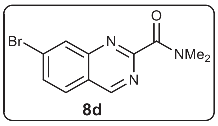

167.44
159.39
159.13
156.80
146.08
130.29
128.21
125.53
103.93
77.48
77.16
76.84
55.99
38.64
35.33
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0


Cl
N
N
O
NMe2

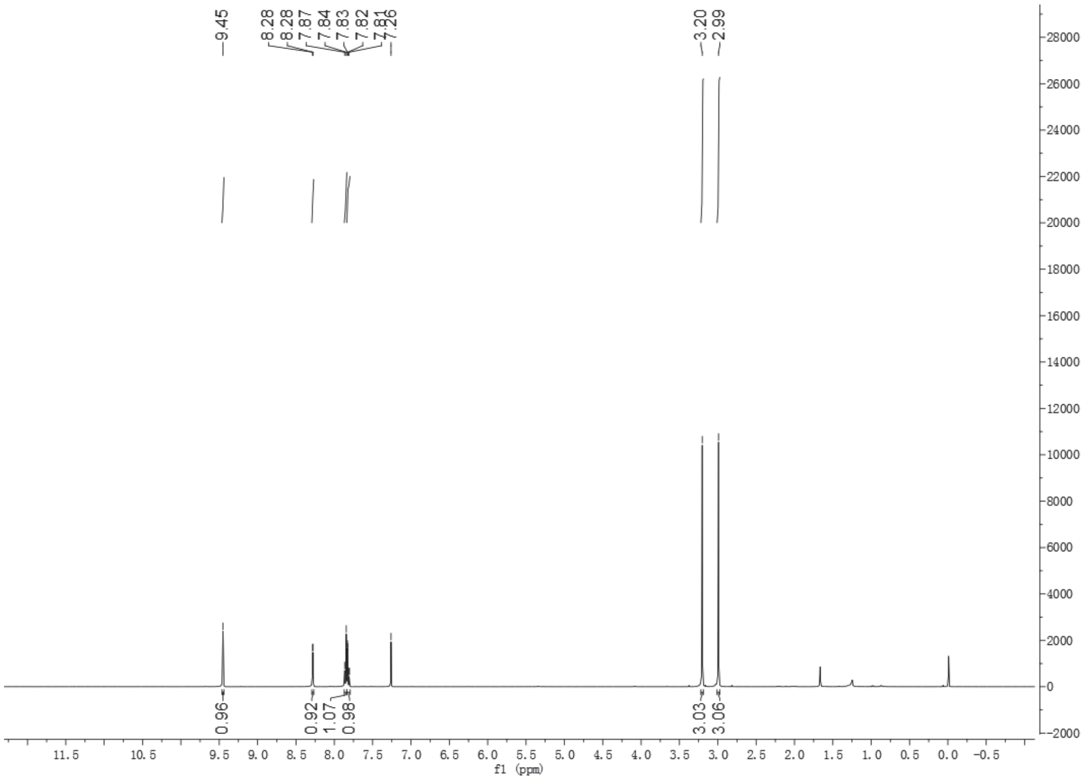
8c

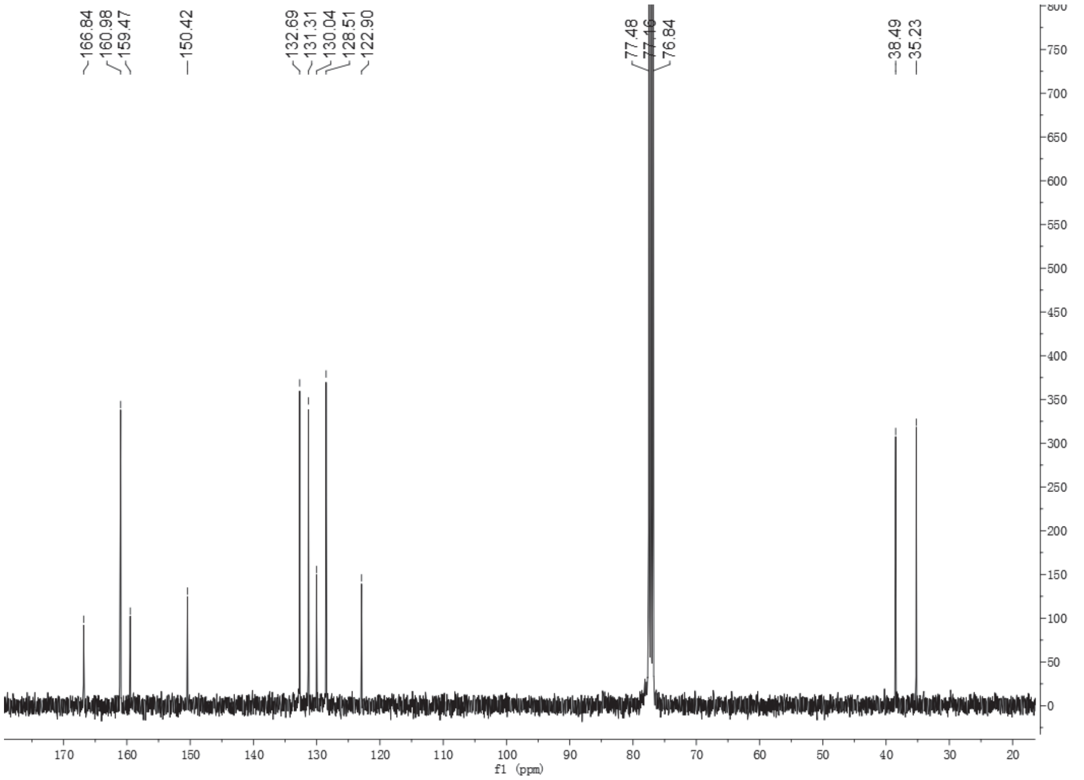

9.46
8.09
8.09
7.96
7.94
7.70
7.70
7.68
7.67
7.28
3.21
3.00
1.05
0.97
1.05
1.01
3.04
3.00
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

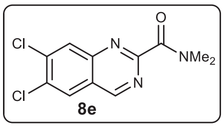

166.84
160.80
159.50
150.33
141.43
130.14
128.64
127.88
122.65
77.48
77.16
76.84
38.47
35.21
9500
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Br
N
N
O
NMe2

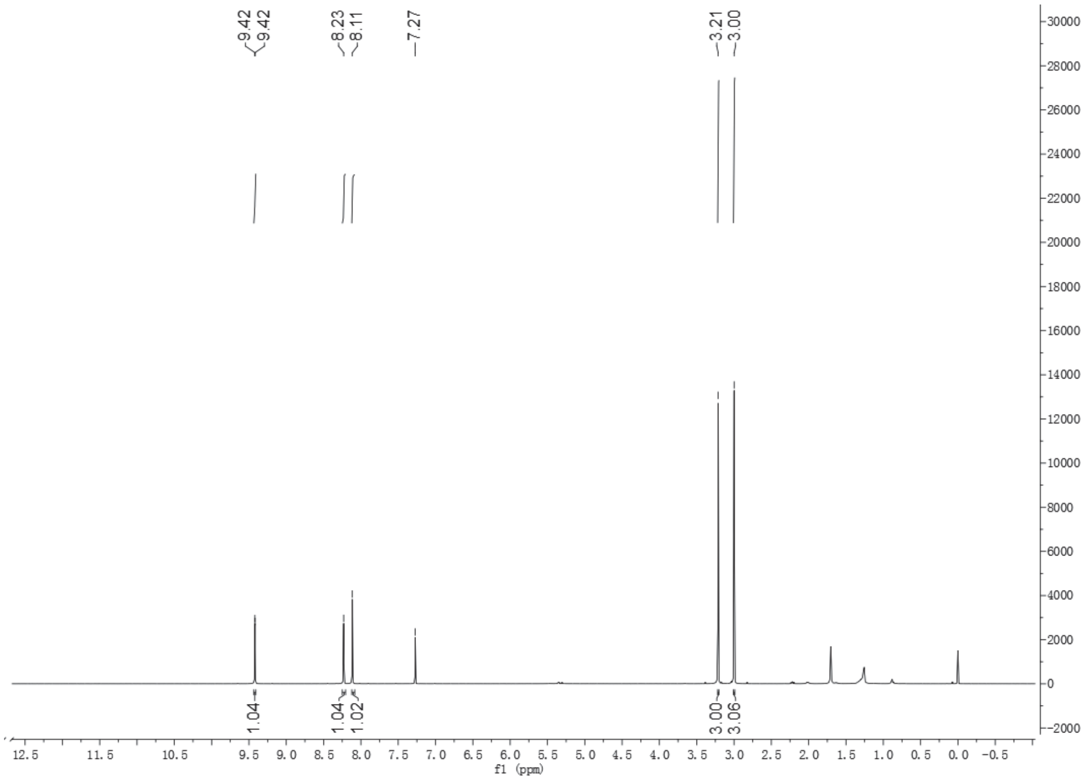
8d

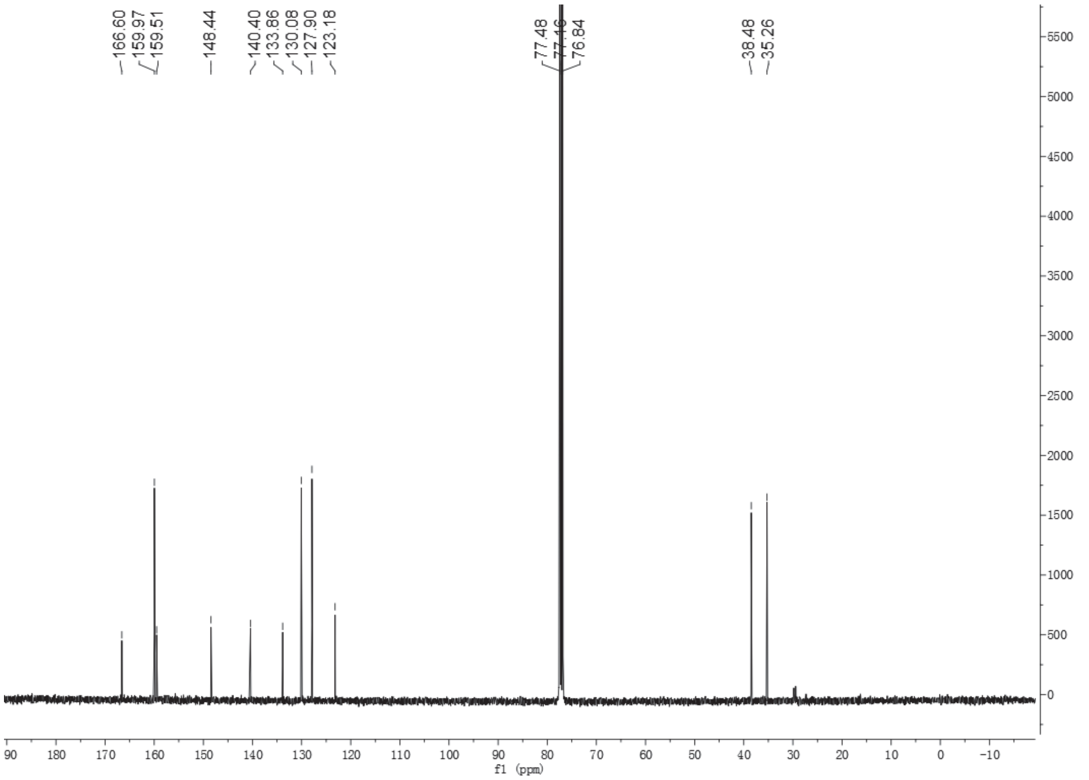

9.45
8.28
8.28
7.87
7.84
7.83
7.82
7.81
7.26
3.20
2.99
0.96
0.92
1.07
0.98
3.03
3.06
f1 (ppm)

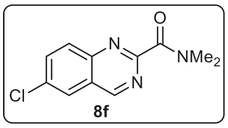

166.84
160.98
159.47
150.42
132.69
131.31
130.04
128.51
122.90
77.48
77.16
76.84
38.49
35.23
f1 (ppm)


Cl
Cl
N
N
O
NMe$_2$

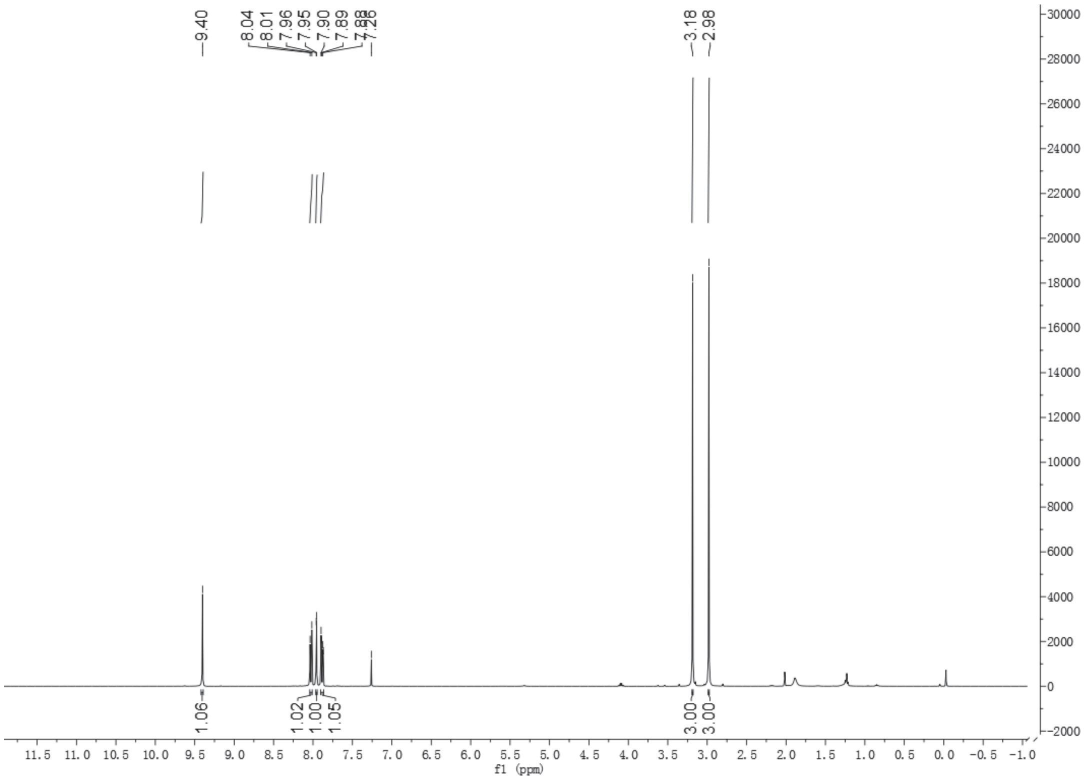
8e

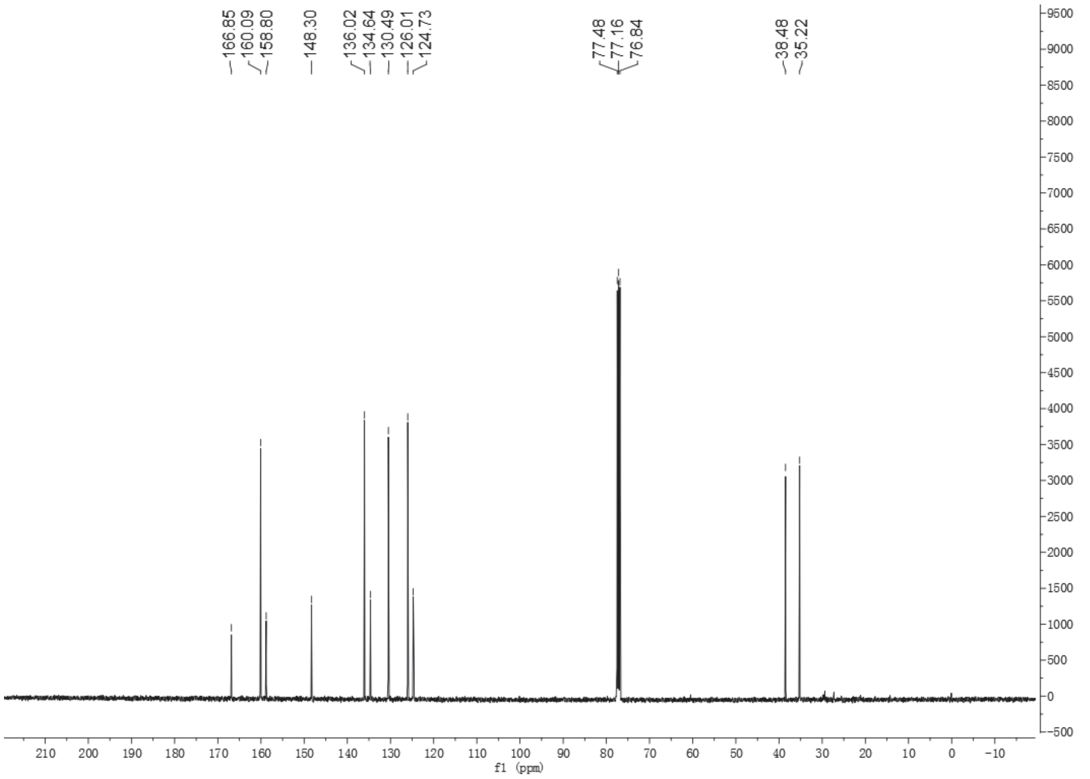

9.42
9.42
8.23
8.11
7.27
3.21
3.00
1.04
1.04
1.02
3.00
3.06
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
−2000
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)


166.60
159.97
159.51
148.44
140.40
133.86
130.08
127.90
123.18
77.48
77.16
76.84
38.48
35.26
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)


O
N
NMe2
N
Cl

8f


9.40
8.04
8.01
7.96
7.95
7.90
7.89
7.88
7.26
3.18
2.98
1.06
1.02
1.00
1.05
3.00
3.00
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


166.85
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158.80
148.30
136.02
134.64
130.49
126.01
124.73
77.48
77.16
76.84
38.48
35.22
9500
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)